

Fig. 1a

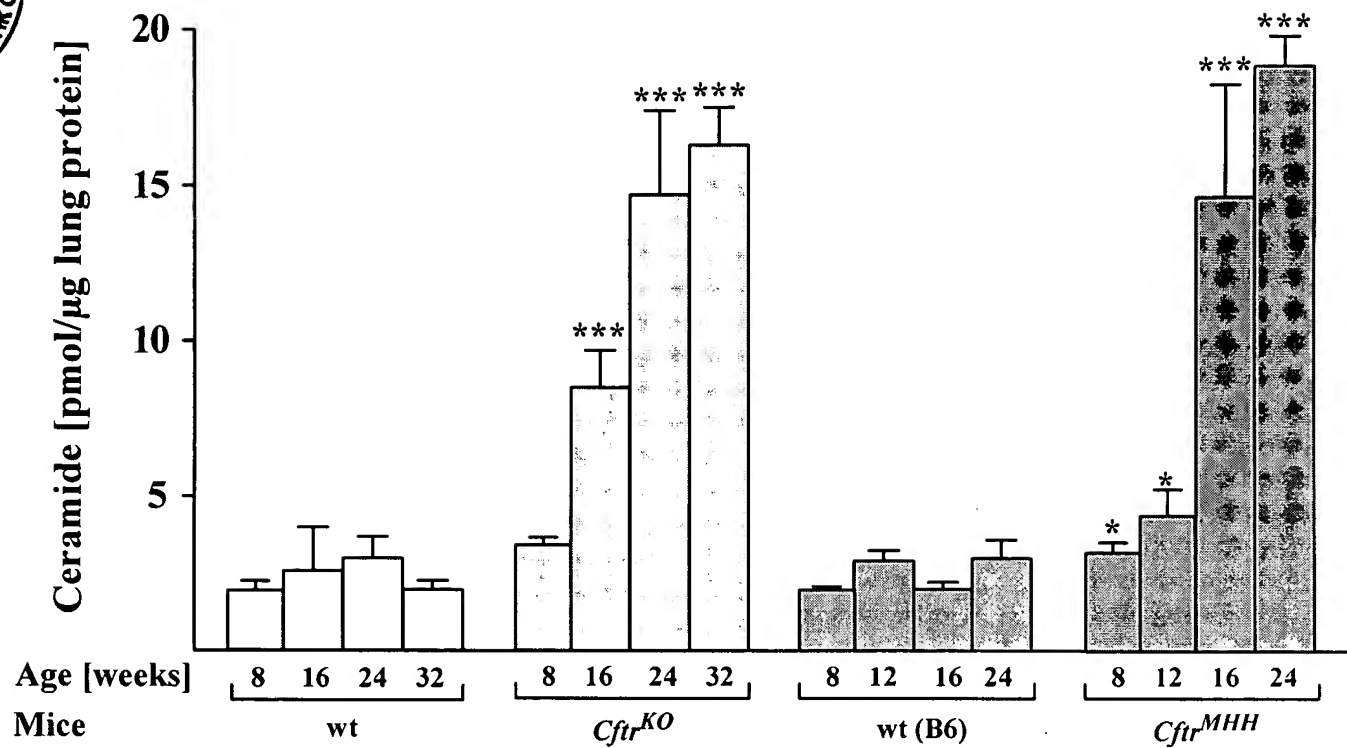
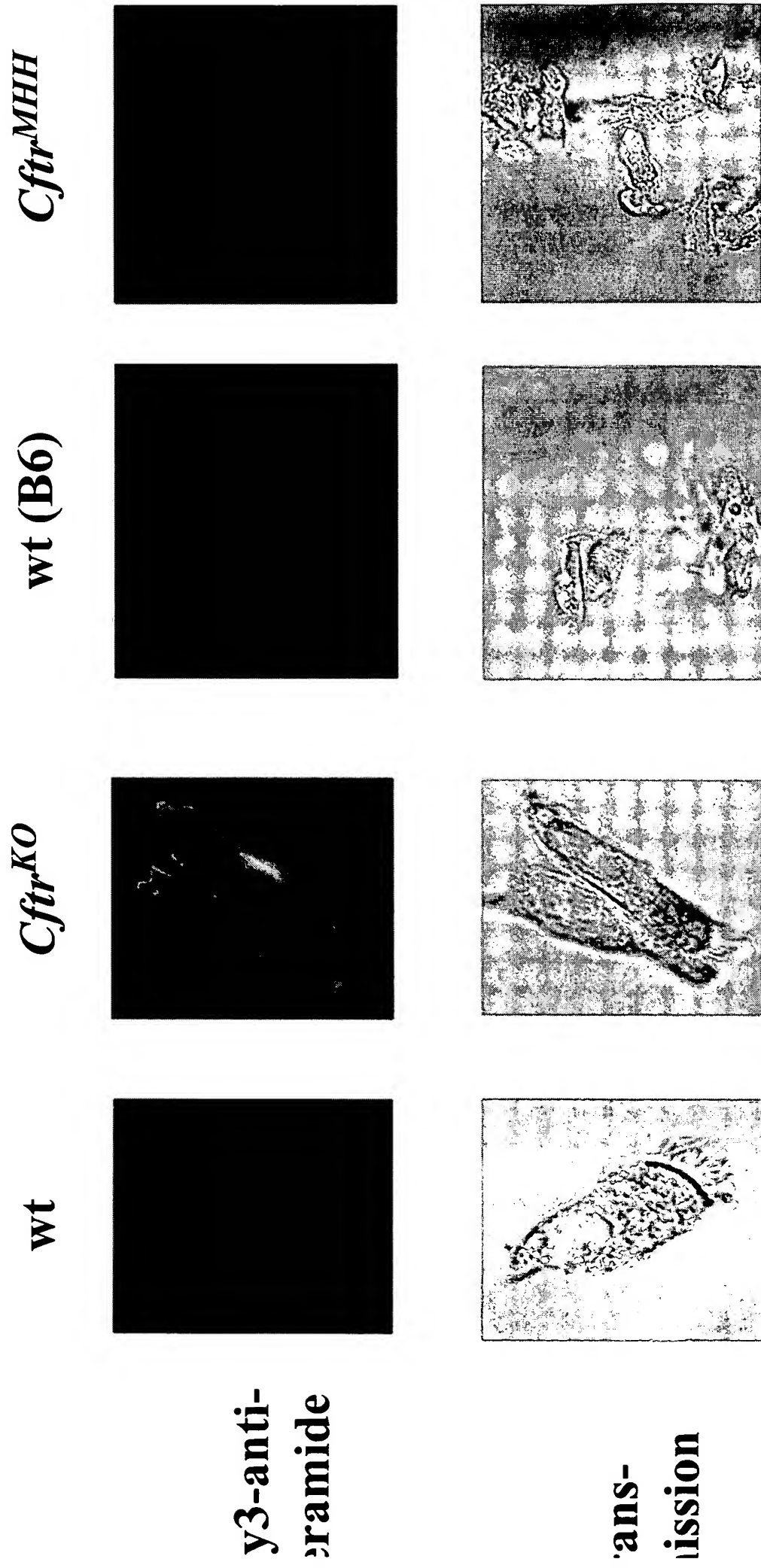


fig. 1b

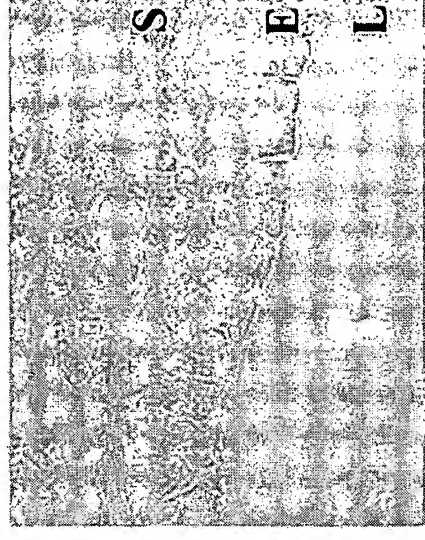
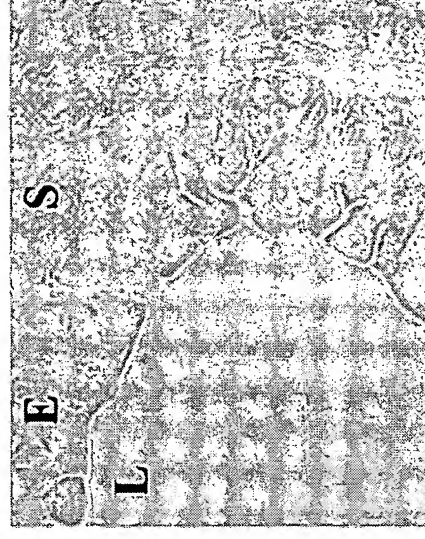
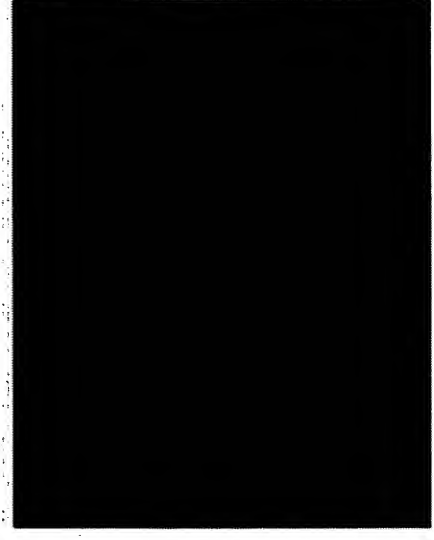
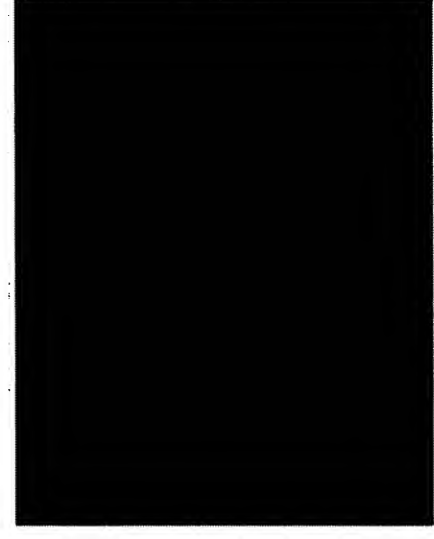
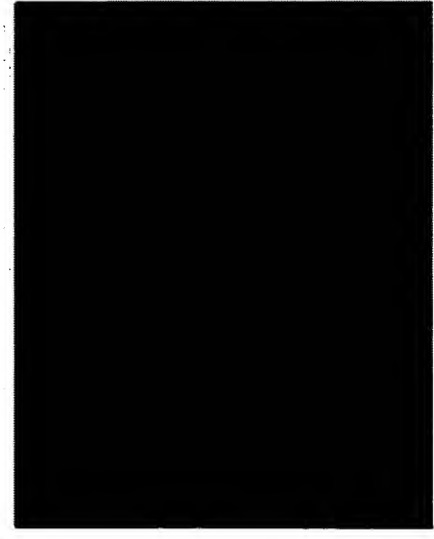


g. 1c

wt

*Cftr<sup>KO</sup>*

*Cftr<sup>MHH</sup>*



Cy3-anti-ceramide

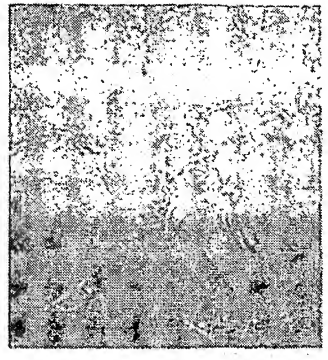
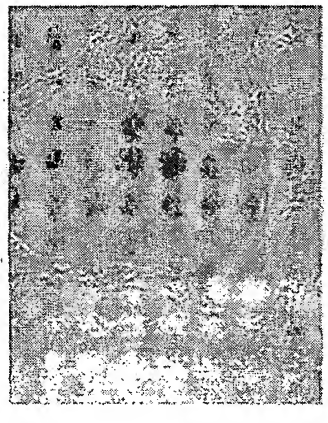
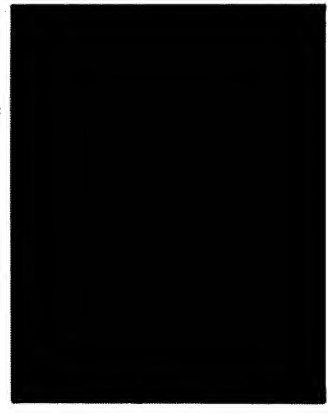
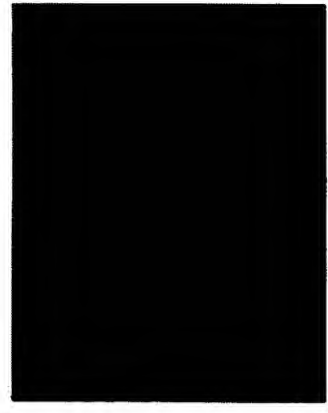
trans-mission

veoli

wt

*Cftr<sup>KO</sup>*

*Cftr<sup>KO</sup>*

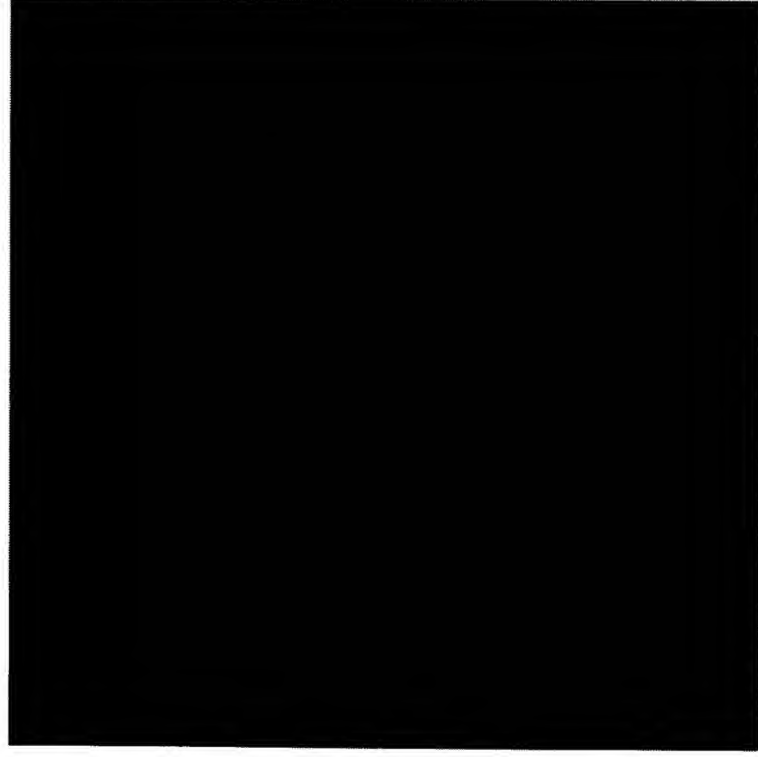


Cy3-anti-ceramide

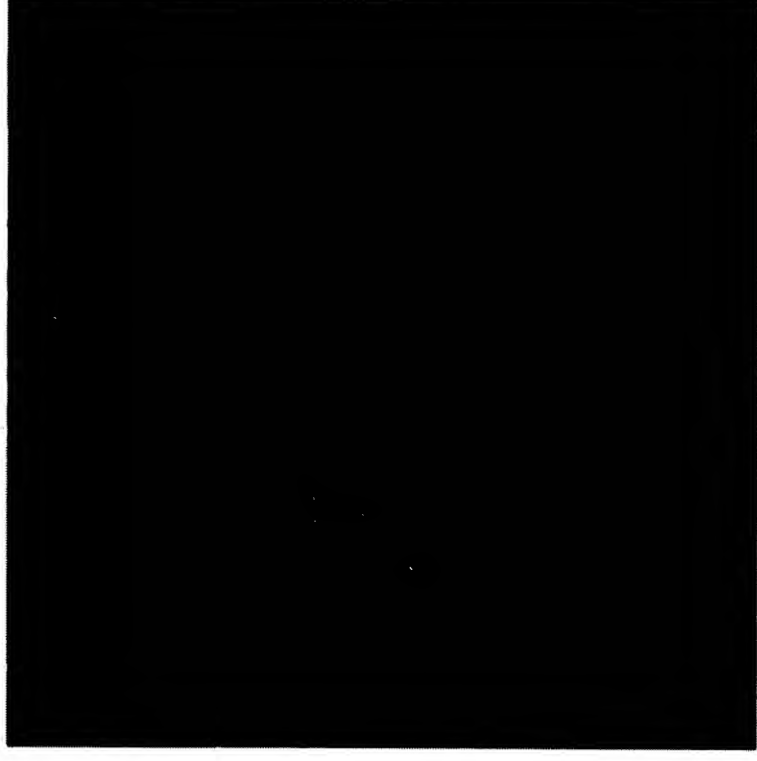
trans-mission

**Fig. 1d**

**wt**

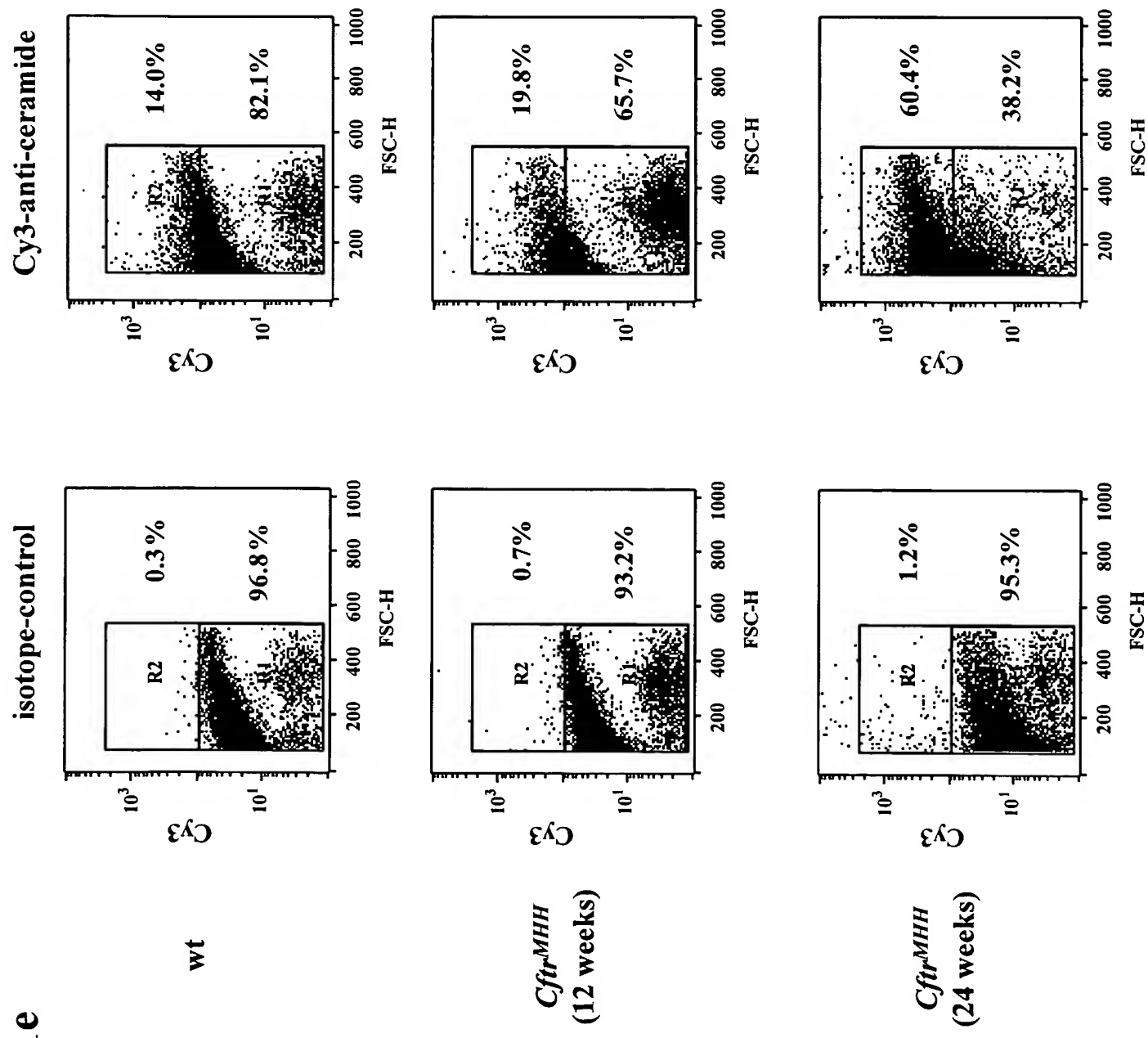


***Cftr<sup>MHH</sup>***



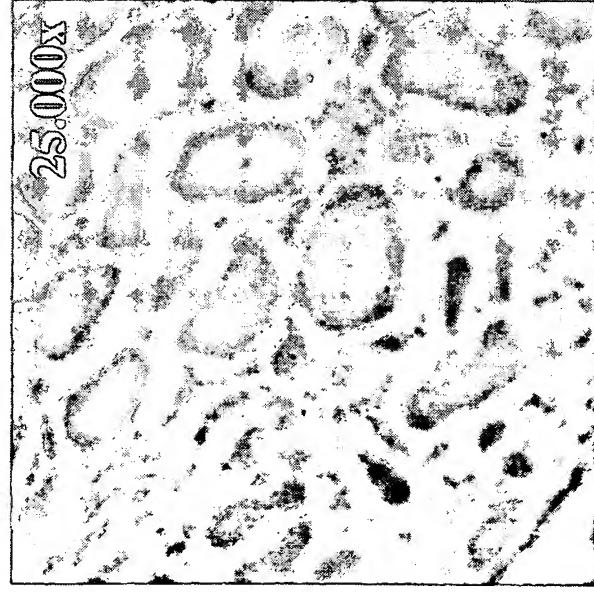
**Cy3-anti-  
ceramide  
(confocal)**

**Fig. 1e**



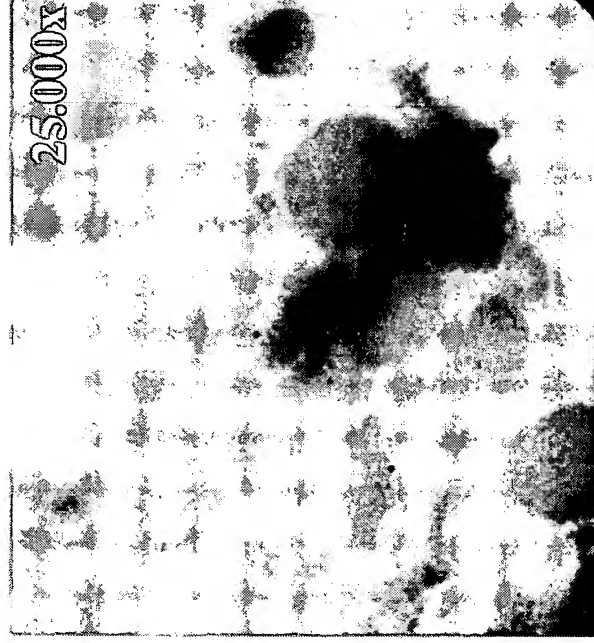
g. 1f

wt



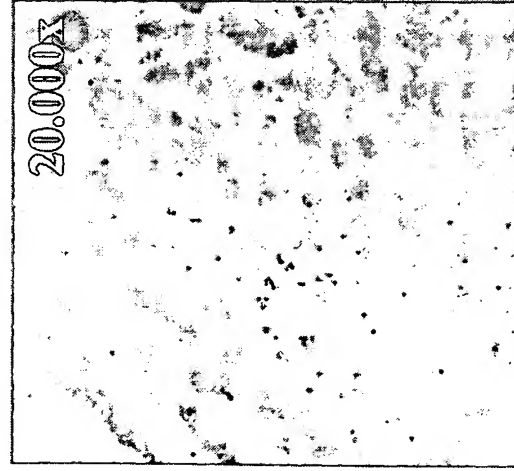
25 nm anti-ceramide

wt



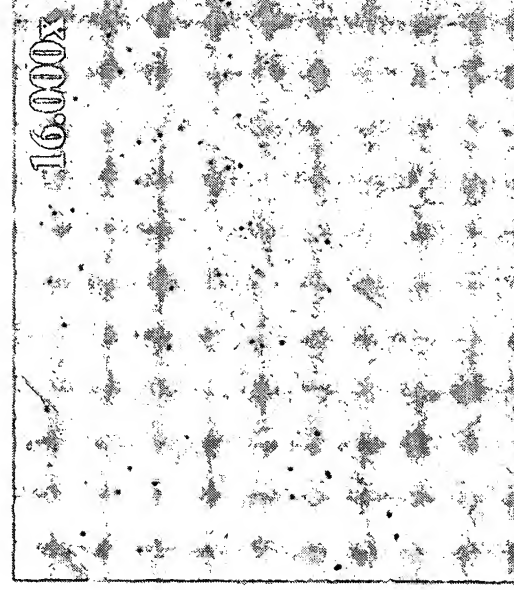
10 nm anti-cathepsin D

*Cfir<sup>MHH</sup>*



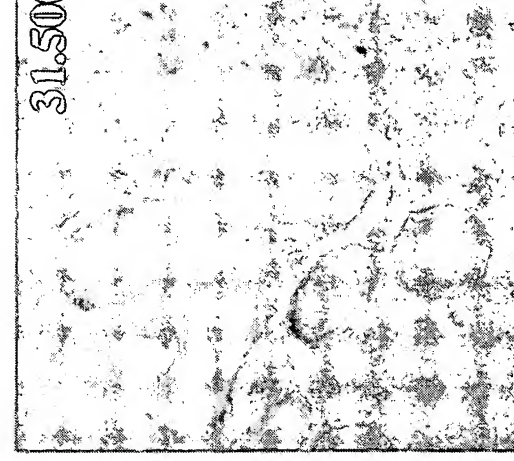
25 nm anti-ceramide

*Cfir<sup>MHH</sup>*



10 nm anti-cathepsin D

*Cfir<sup>MHH</sup>*



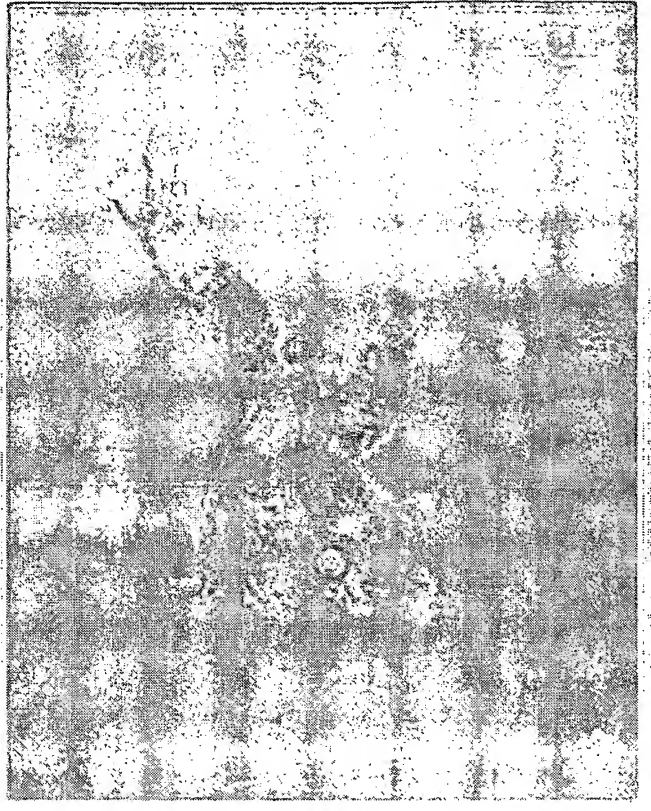
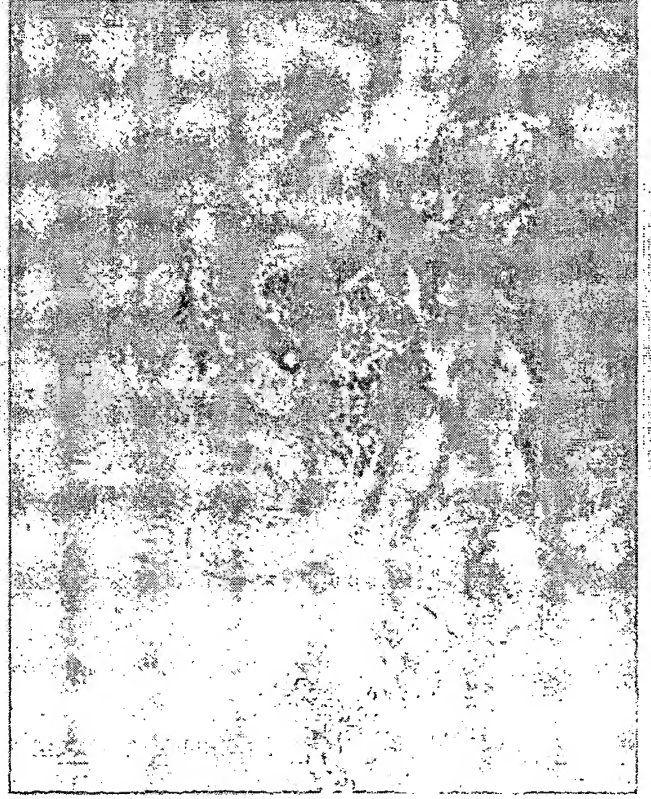
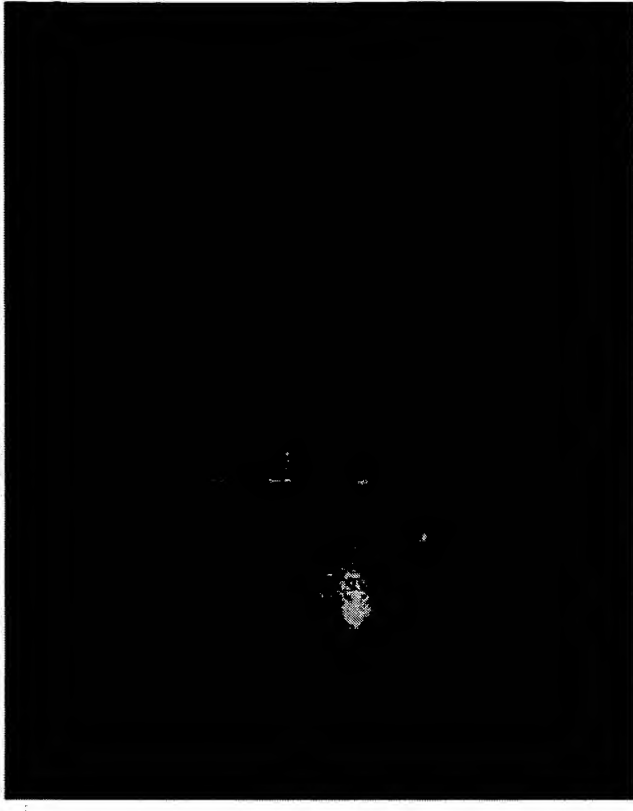
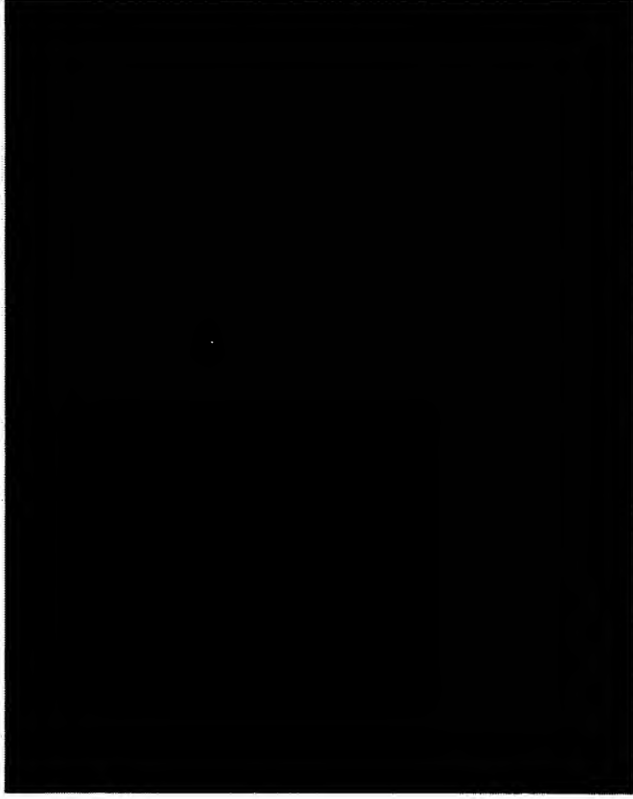
control

Fig. 1g

Cy3-anti-  
ceramide

Control

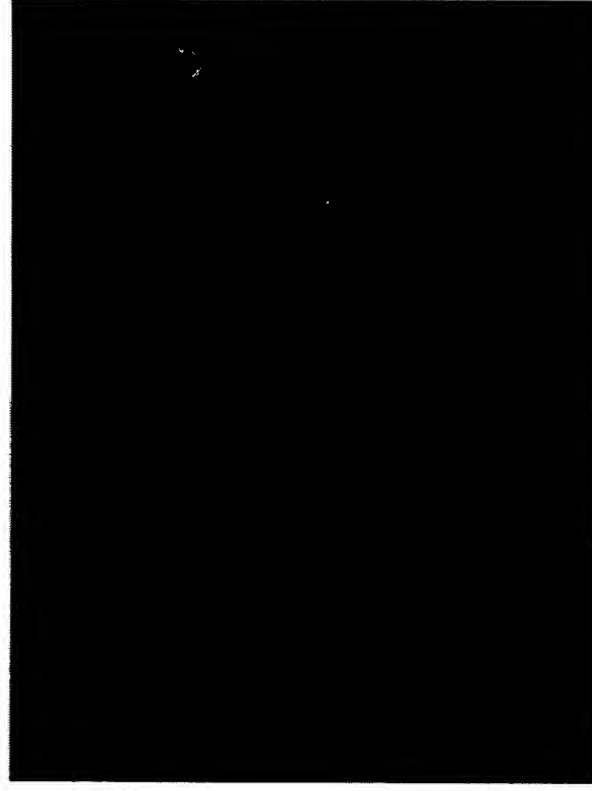
CF-patient



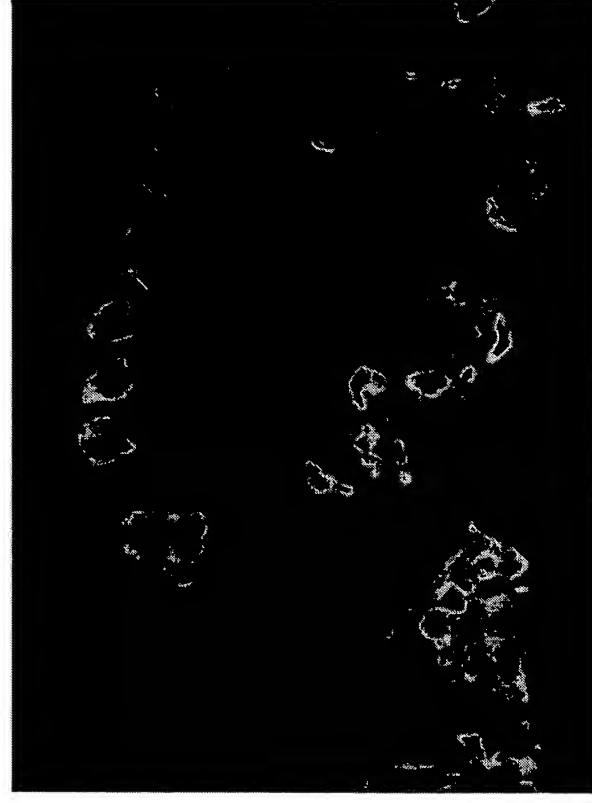
trans-  
mission

**Fig. 1h**

**Control**

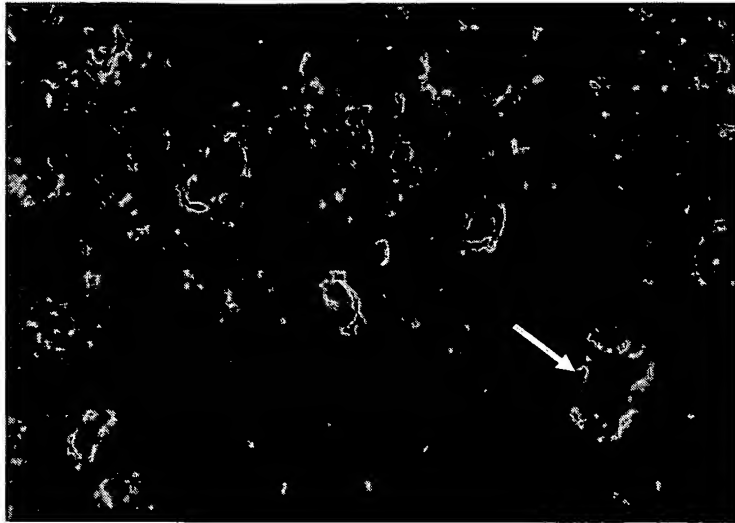


**CF-patient**





**CF-patient**

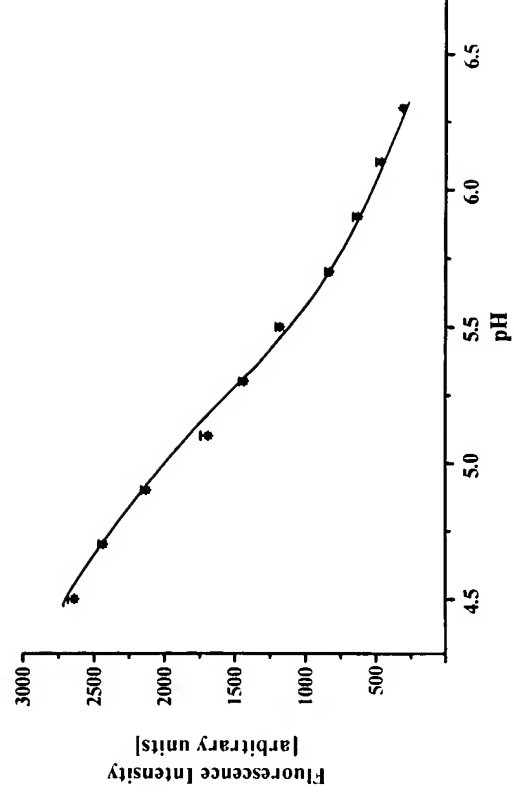
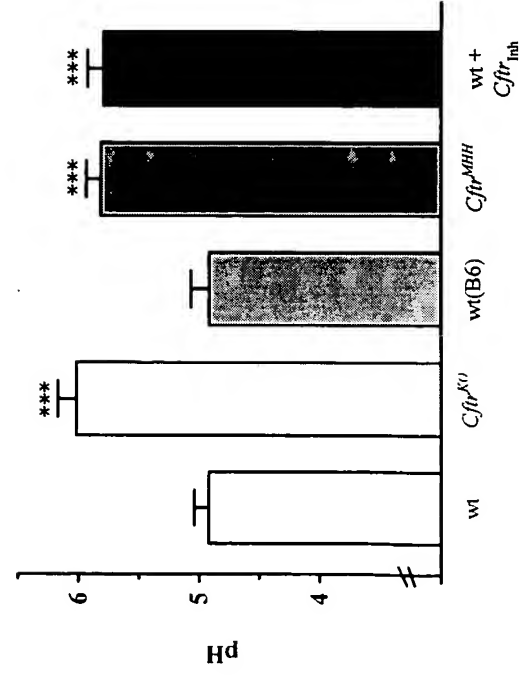
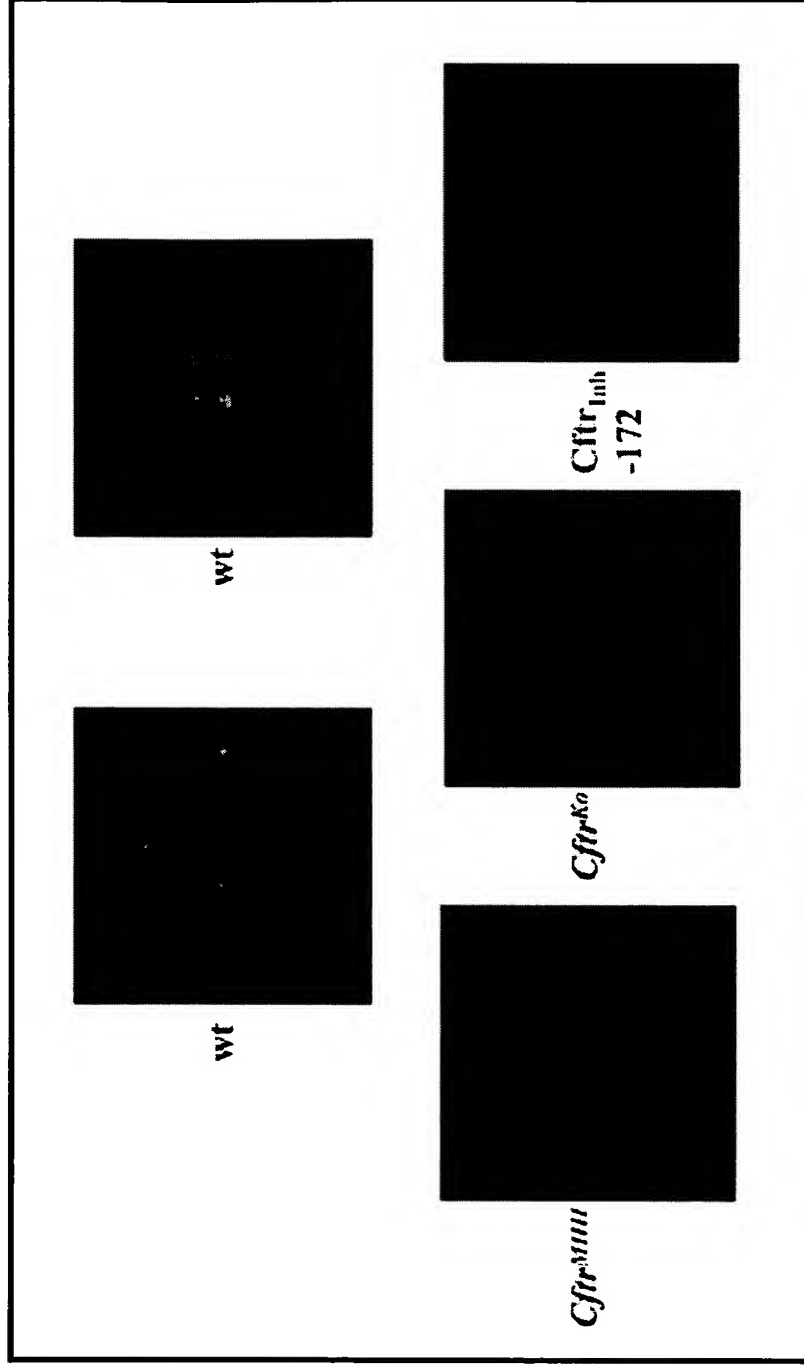


**control**

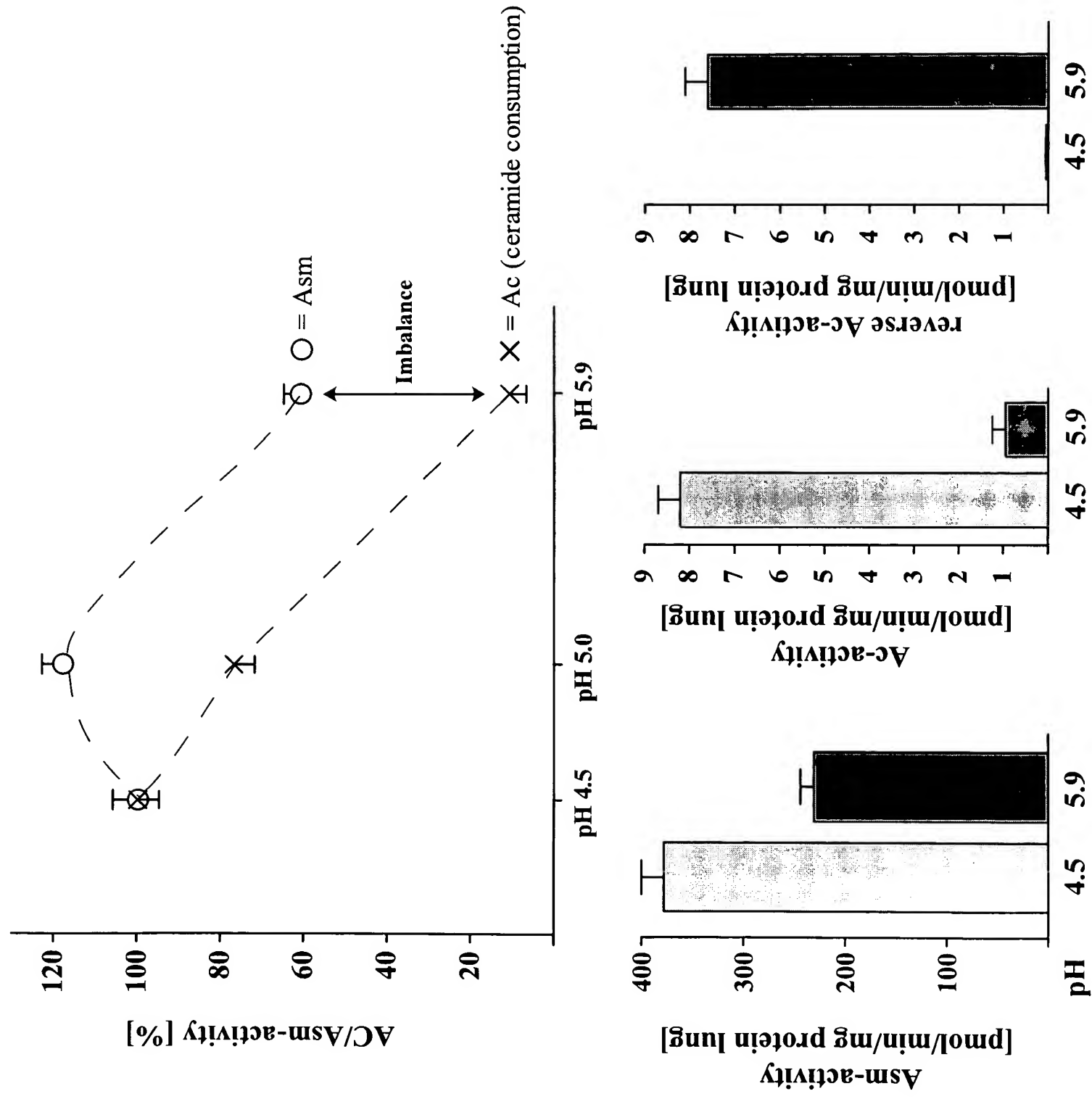


**Staining: FITC-anti ceramide**

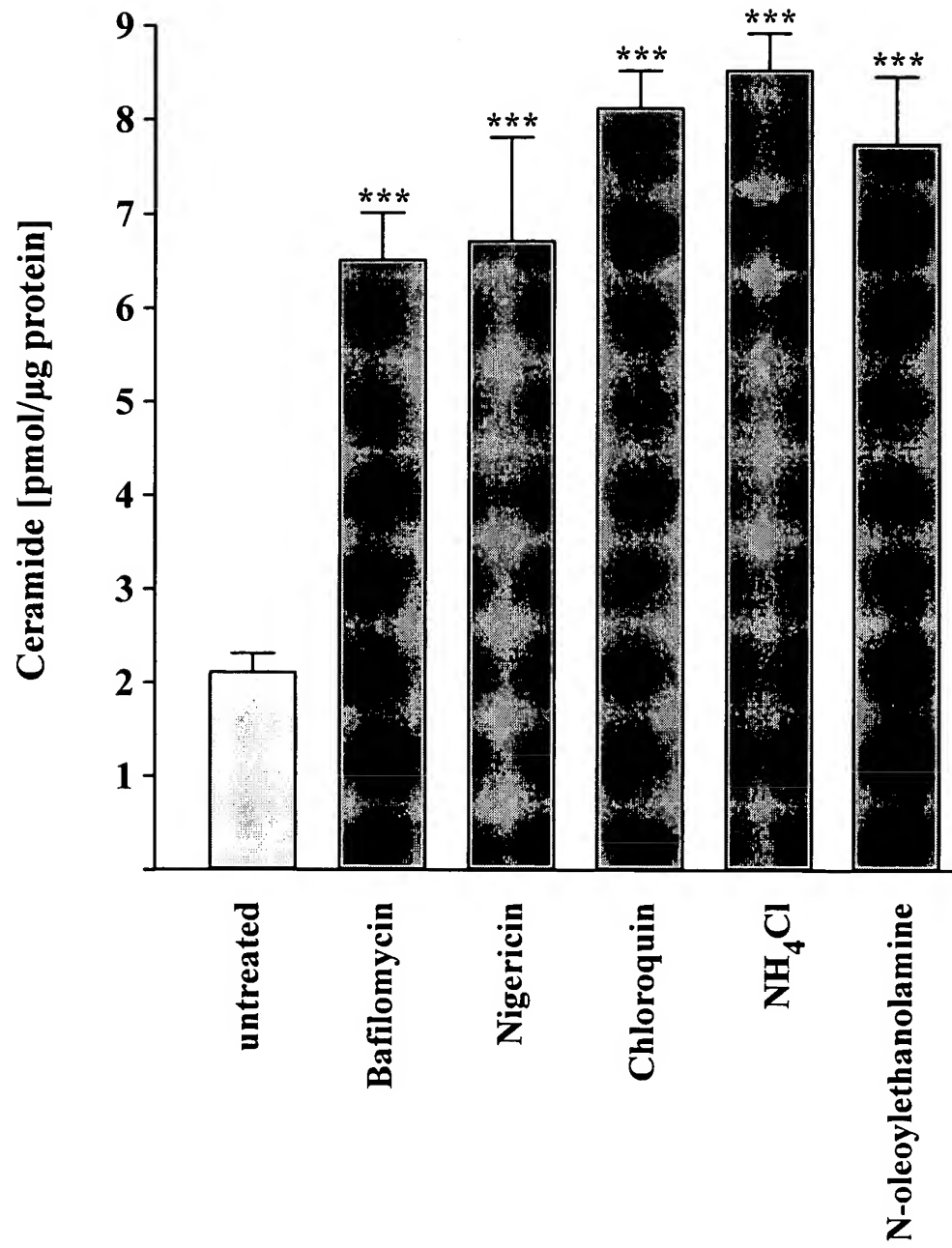
Fig. 2a

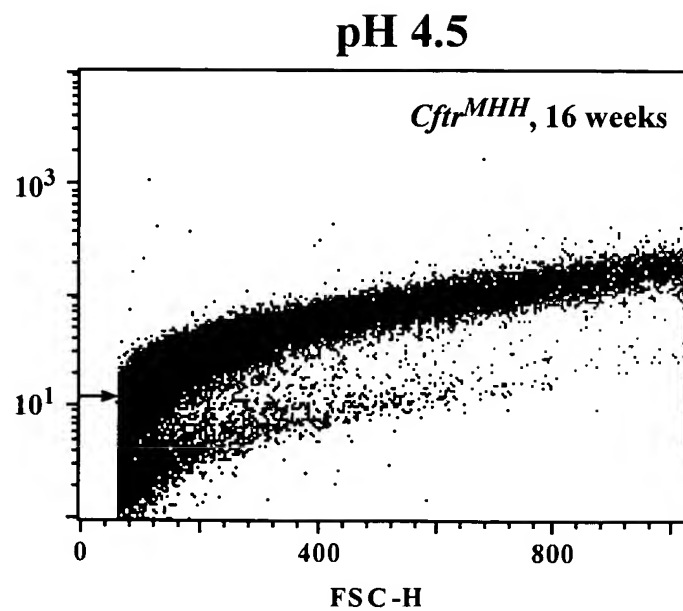
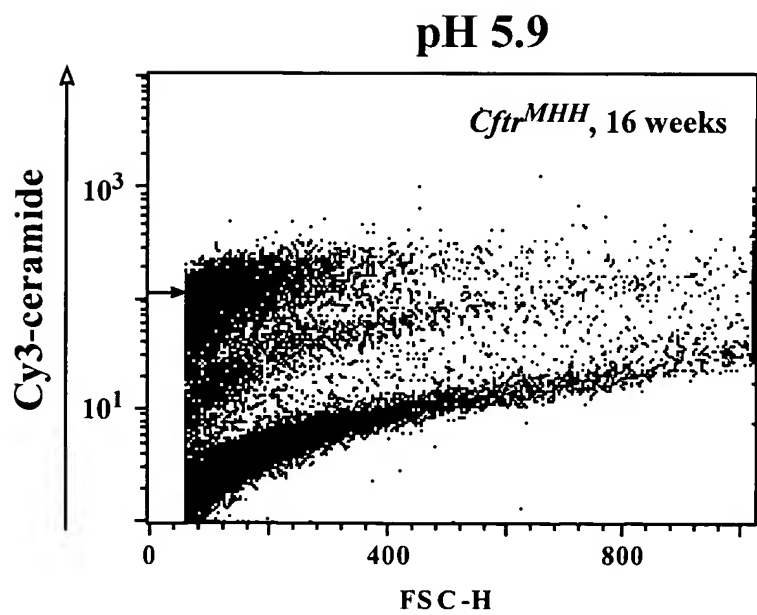
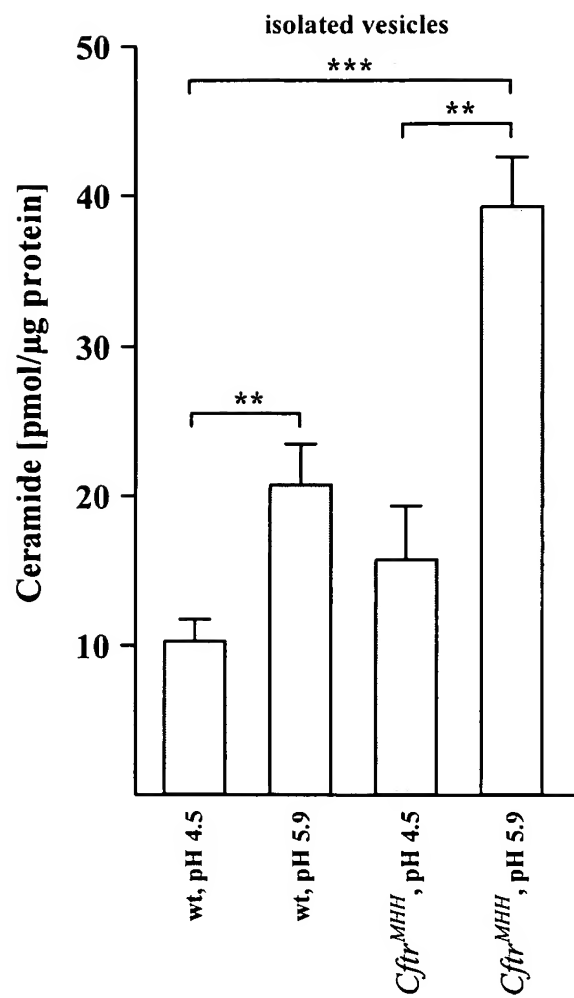


ig. 2b

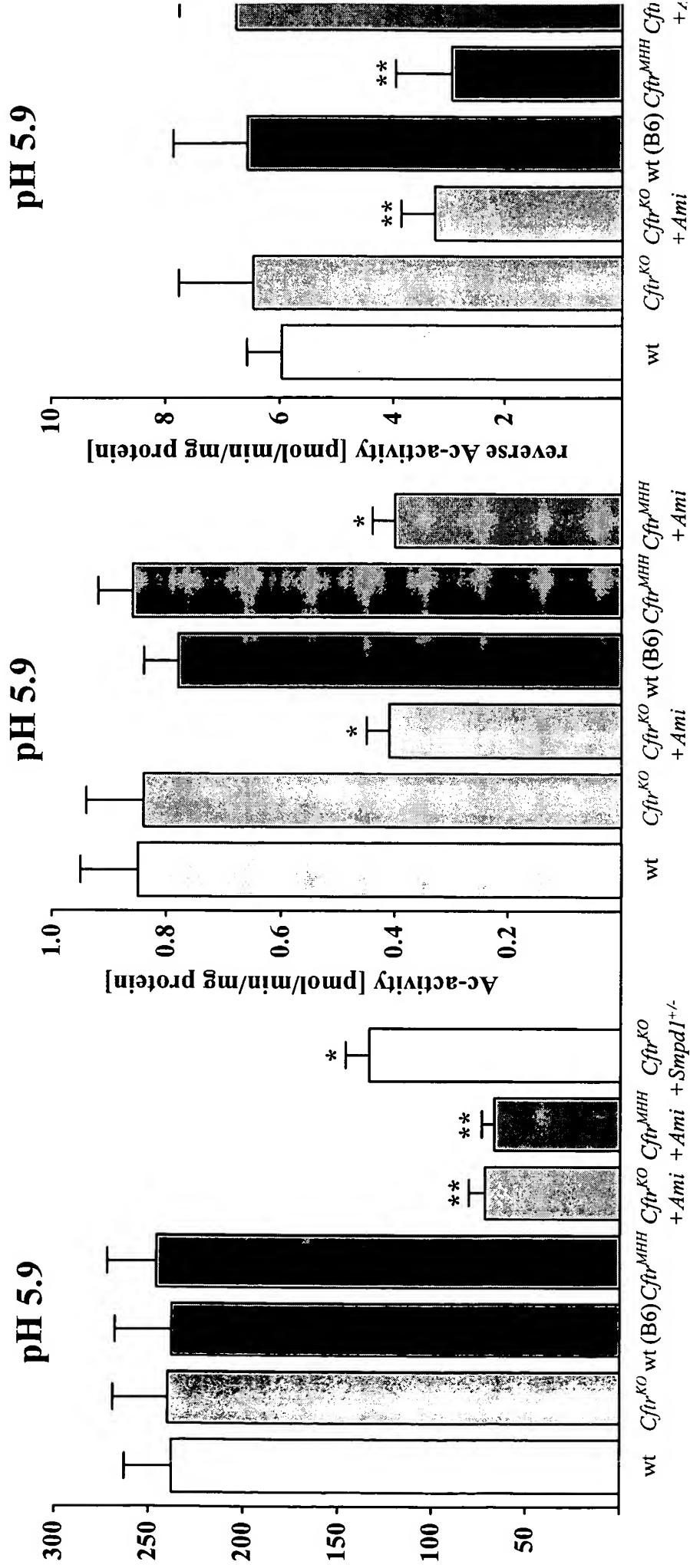


**Fig. 2c**

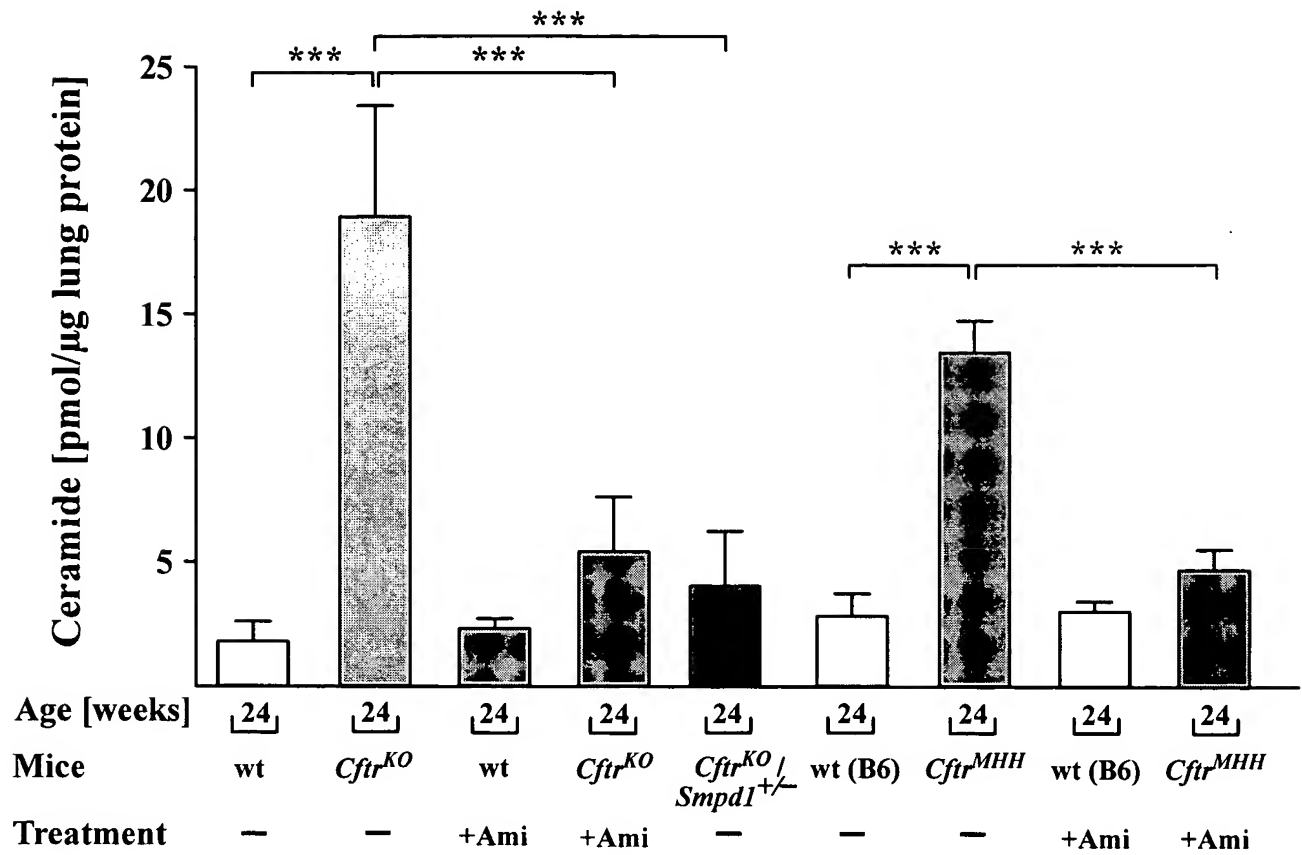




ig. 2e



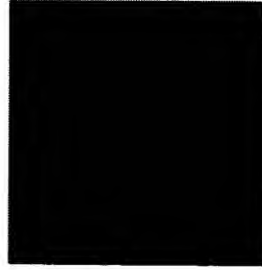
**Fig. 21**



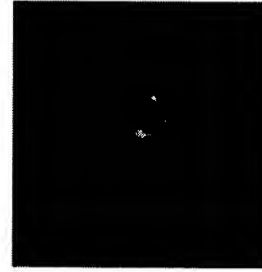
**Fig. 2g**

**Cy3-anti-  
ceramide**

wt



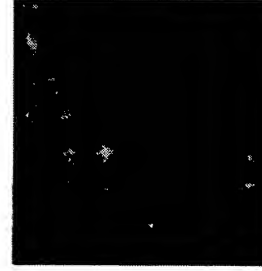
*Cftr*<sup>KO</sup>



wt (B6)



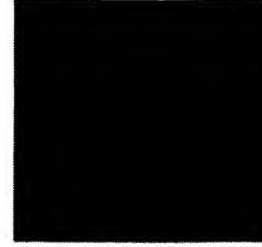
*Cftr*<sup>MHH</sup>



*Cftr*<sup>KO</sup>  
*Smpd1*<sup>+/+</sup>



*Cftr*<sup>MHH</sup>  
+Ami



**trans-  
mission**

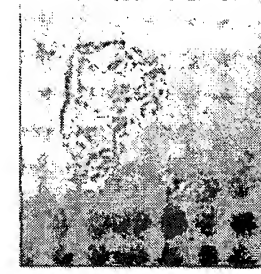
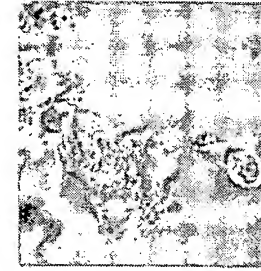
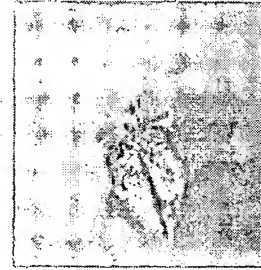
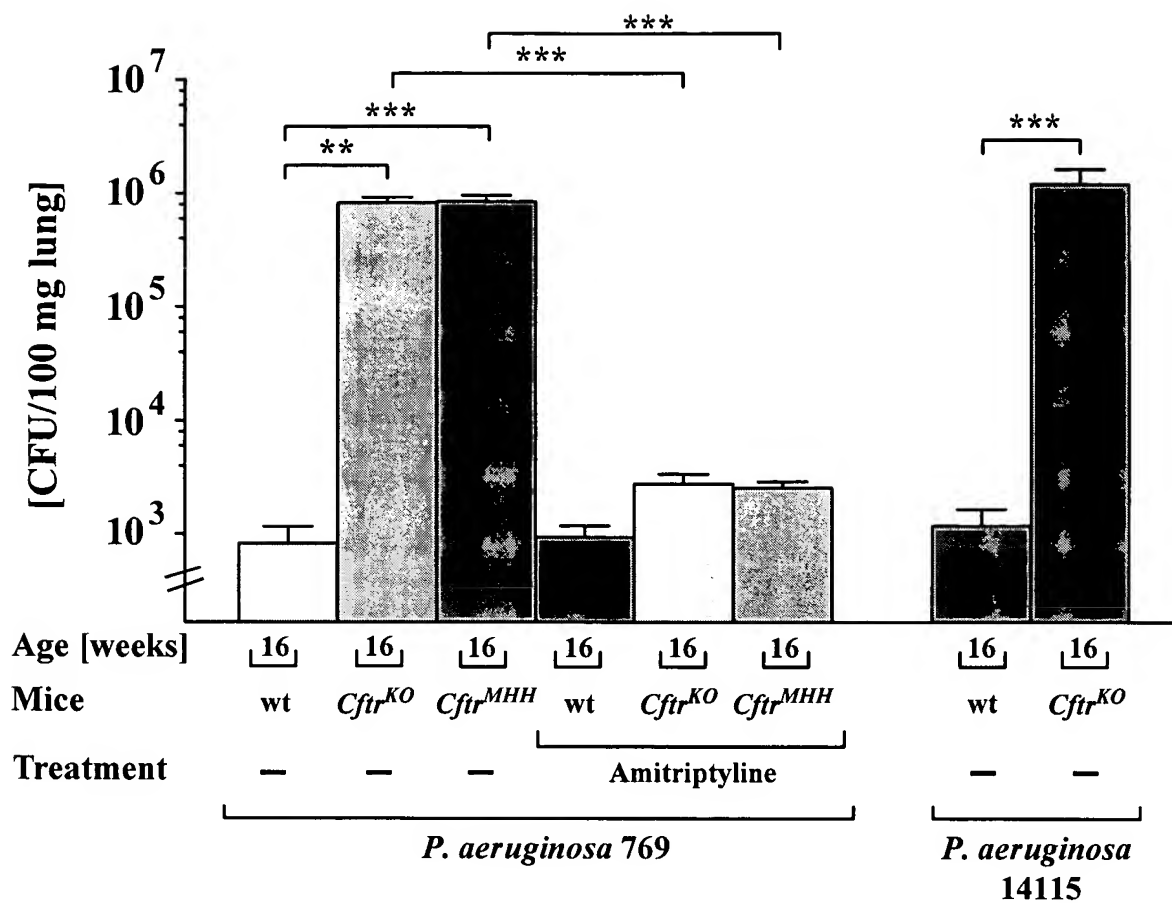


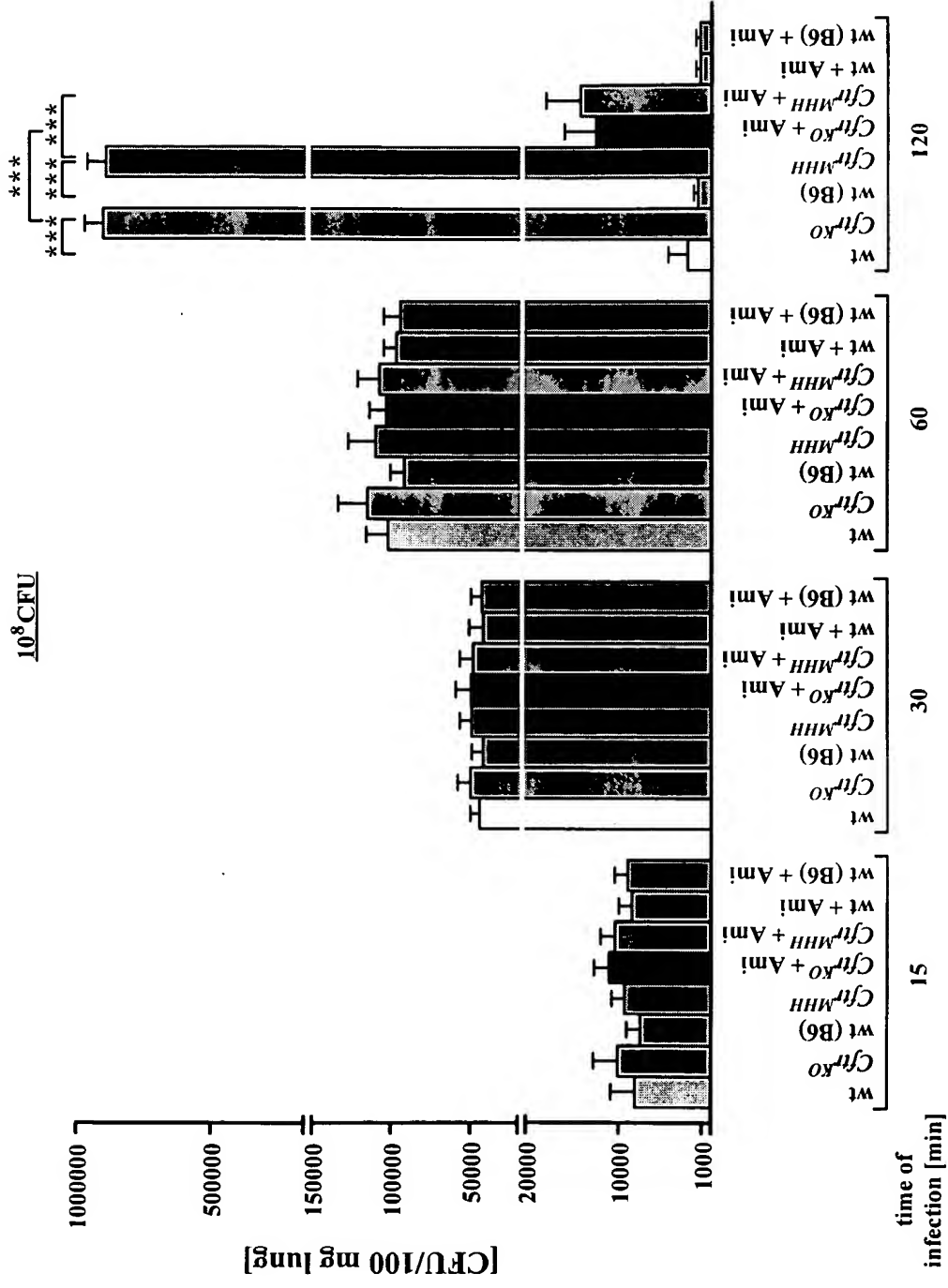


Figure 3 is a bar graph showing airway hyperresponsiveness (AHR) in Cfr<sup>KO</sup> mice. The y-axis represents [CRU/100 mg lung] on a logarithmic scale from 10<sup>3</sup> to 10<sup>7</sup>. The x-axis shows age (weeks) and treatment (+Ami or -). The graph compares wt, Cfr<sup>KO</sup>, and Cfr<sup>MHH</sup> mice, with and without Smpd1<sup>+/-</sup> genotype. Statistical significance is indicated by asterisks (\*, \*\*\*) and brackets.

Genotype	Age (weeks)	Treatment	[CRU/100 mg lung]
wt	16	-	~10 <sup>3.2</sup>
		+Ami	~10 <sup>3.5</sup>
		-	~10 <sup>3.8</sup>
	24	-	~10 <sup>3.5</sup>
		+Ami	~10 <sup>3.8</sup>
		-	~10 <sup>4.2</sup>
Cfr <sup>KO</sup>	16	-	~10 <sup>3.5</sup>
		+Ami	~10 <sup>3.8</sup>
		-	~10 <sup>4.2</sup>
	24	-	~10 <sup>3.8</sup>
		+Ami	~10 <sup>4.2</sup>
		-	~10 <sup>4.5</sup>
Cfr <sup>MHH</sup>	16	-	~10 <sup>3.8</sup>
		+Ami	~10 <sup>4.2</sup>
		-	~10 <sup>4.5</sup>
	24	-	~10 <sup>4.2</sup>
		+Ami	~10 <sup>4.5</sup>
		-	~10 <sup>4.8</sup>
Smpd1 <sup>+/-</sup>	16	-	~10 <sup>3.5</sup>
		+Ami	~10 <sup>3.8</sup>
		-	~10 <sup>4.2</sup>
	24	-	~10 <sup>3.8</sup>
		+Ami	~10 <sup>4.2</sup>
		-	~10 <sup>4.5</sup>

**Fig. 3b**





**Fig. 3d**

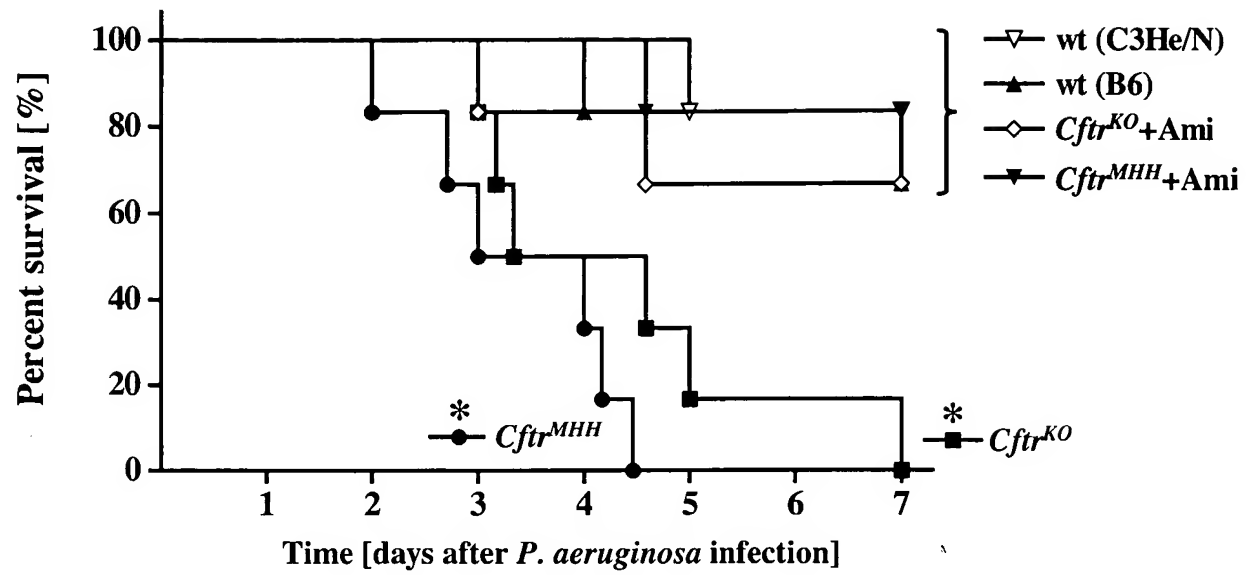


Fig. 4a

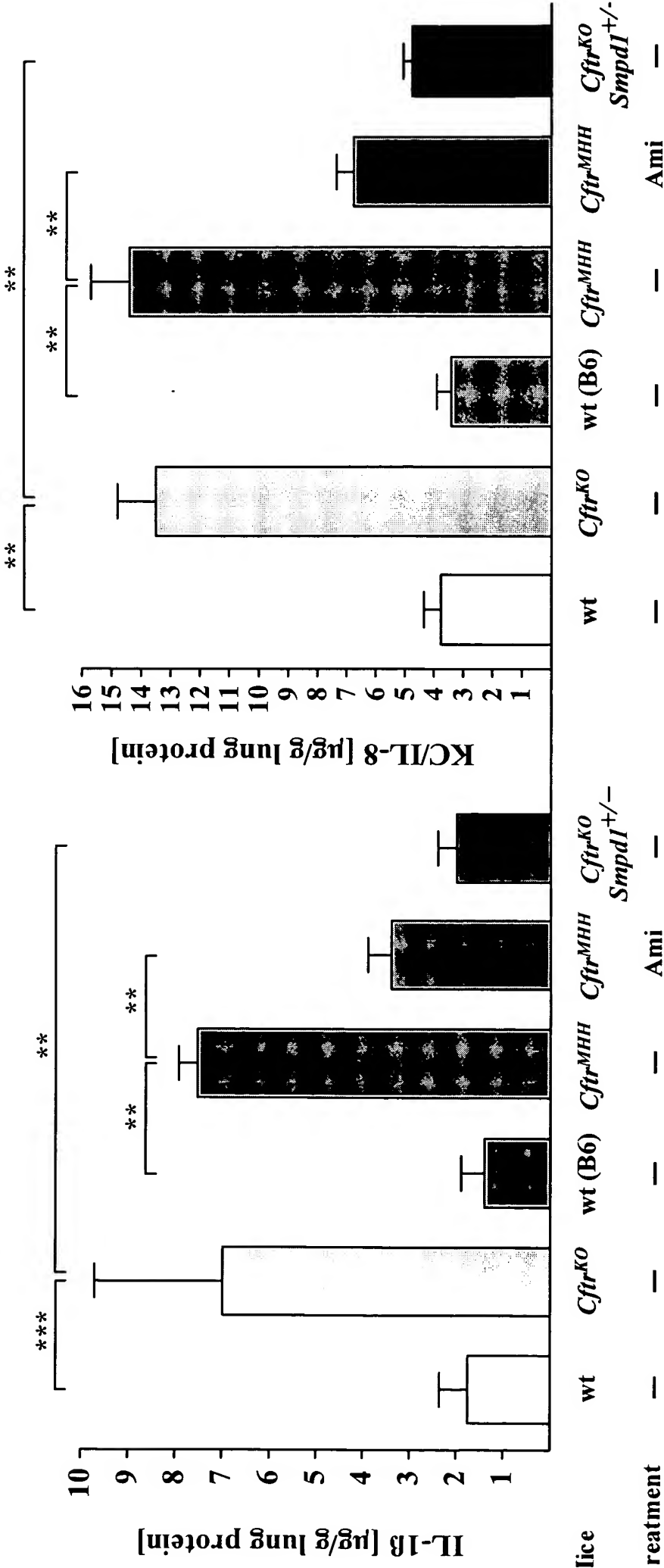


Fig. 4b

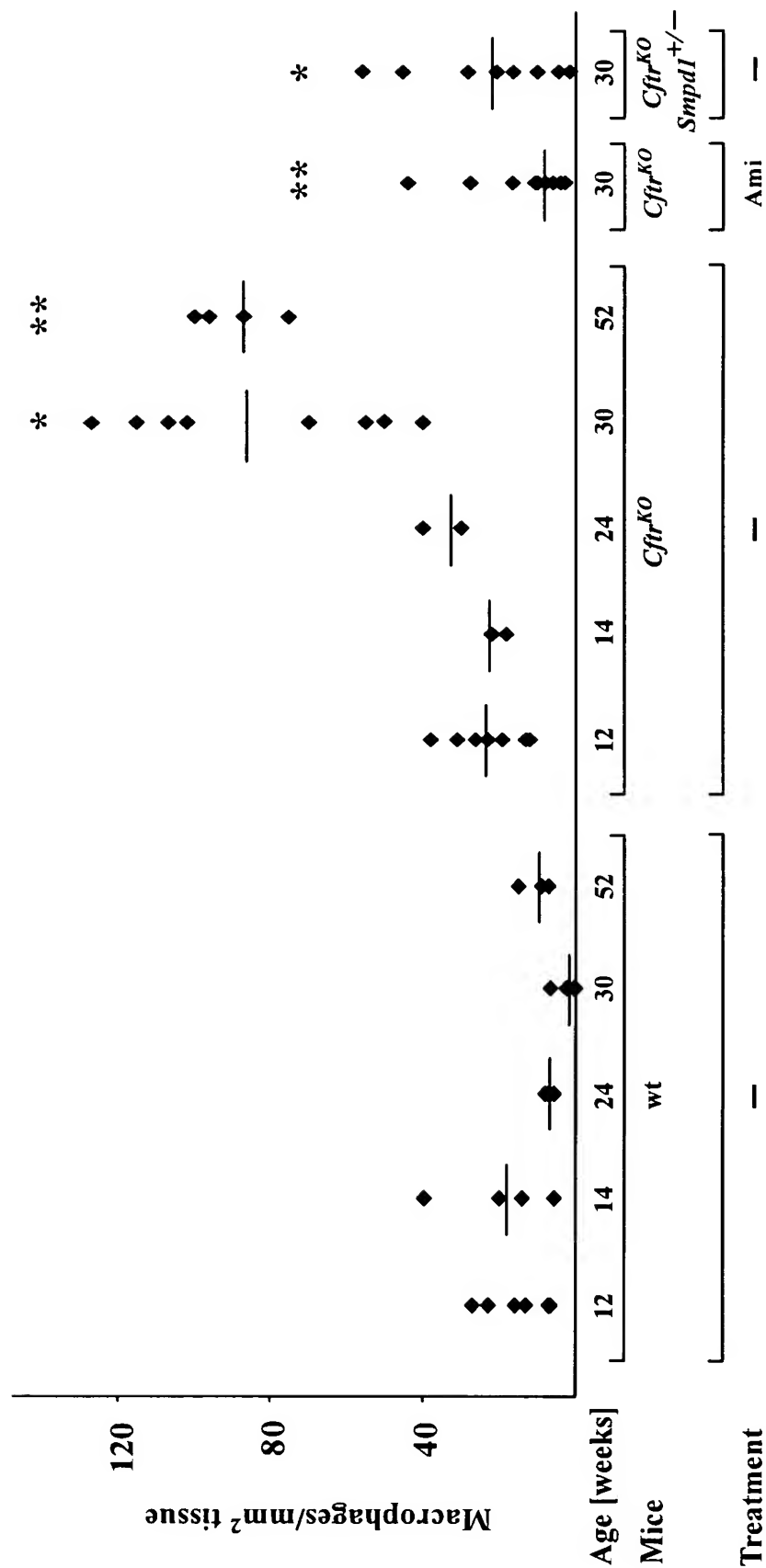
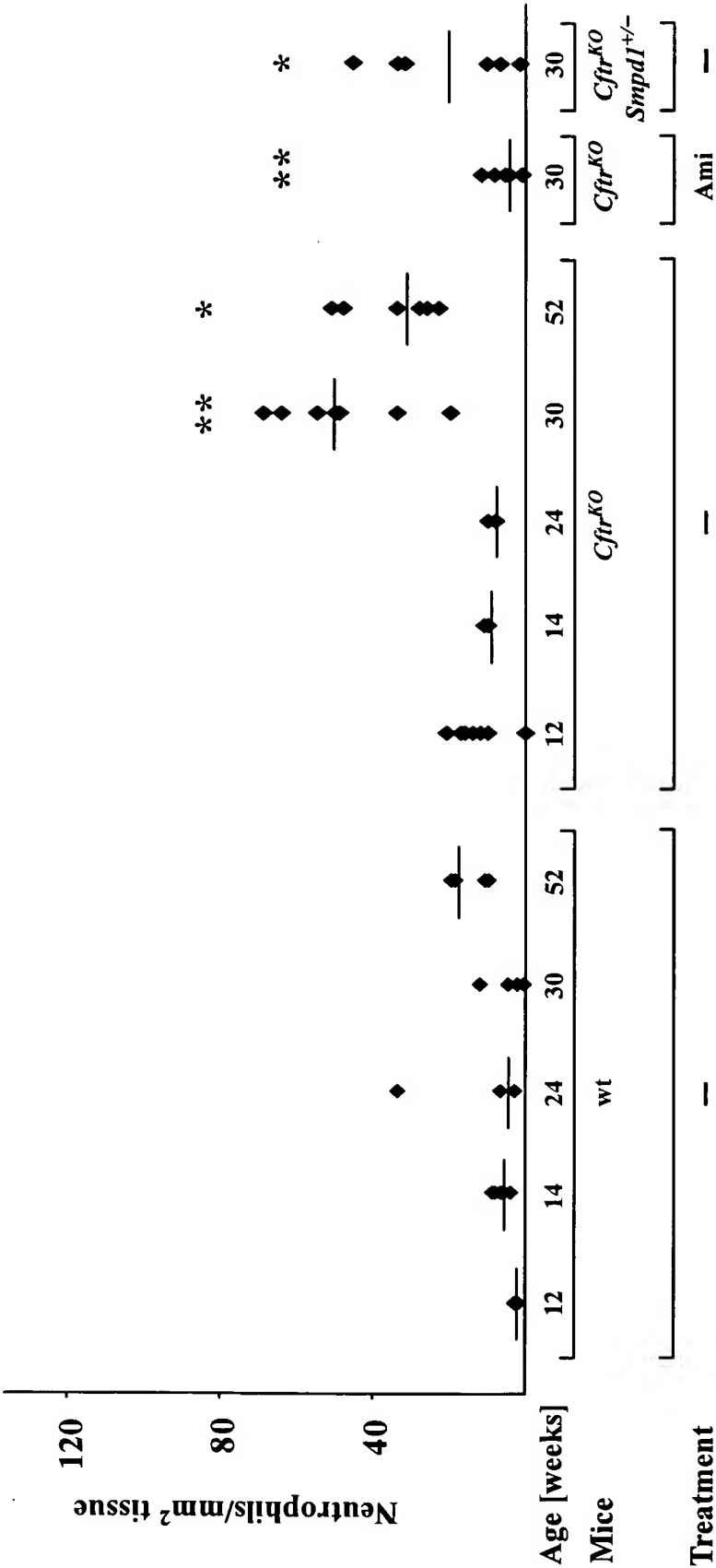
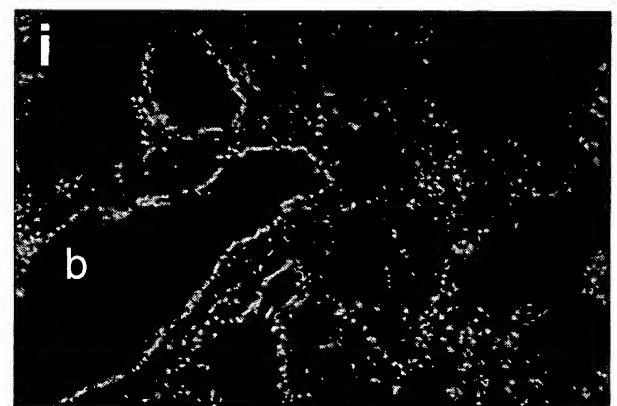
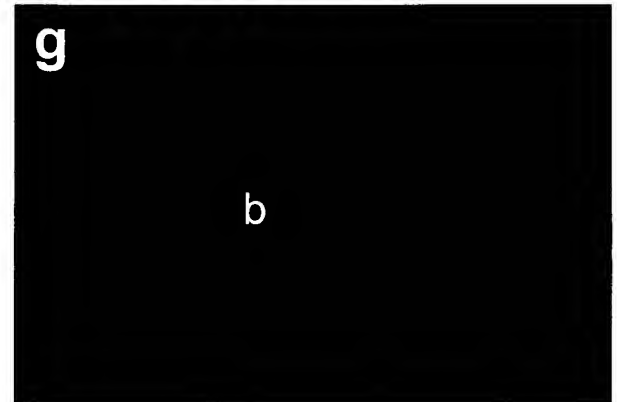
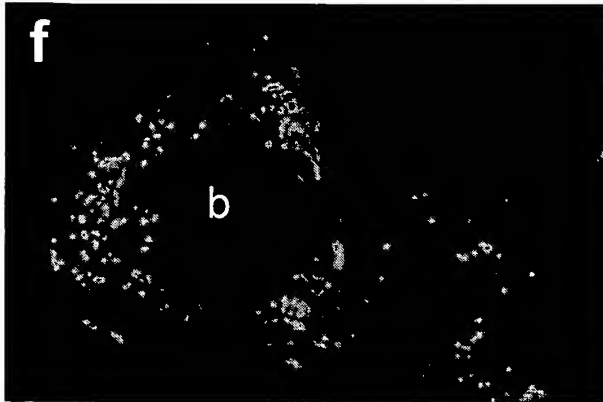
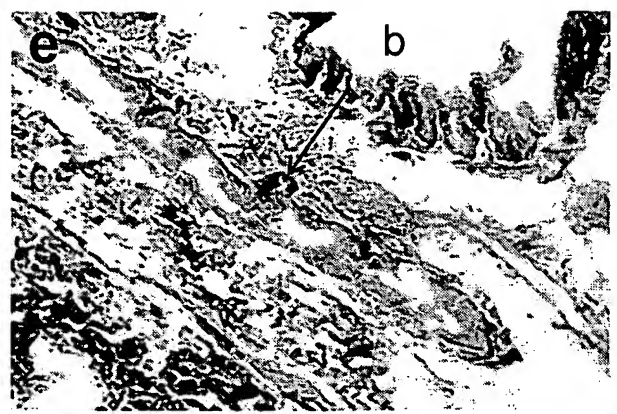
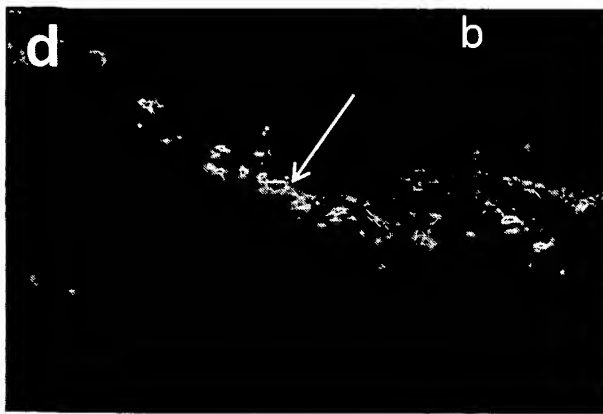


Fig. 4c

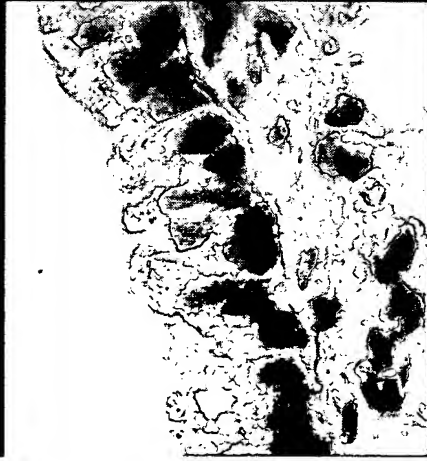




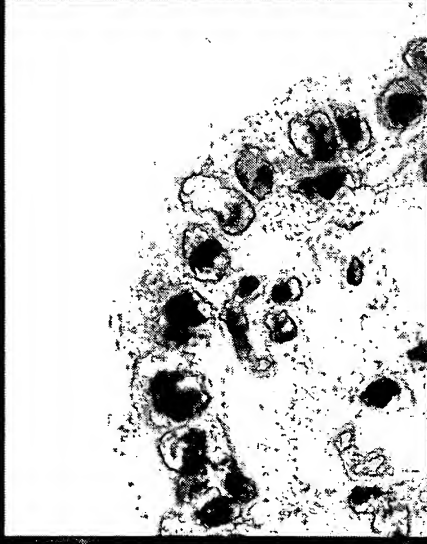


g. 5a

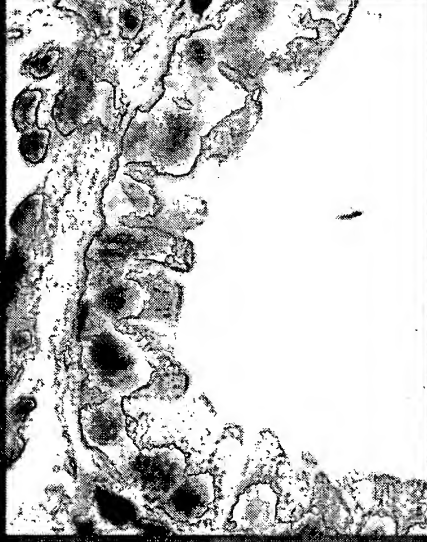
wt



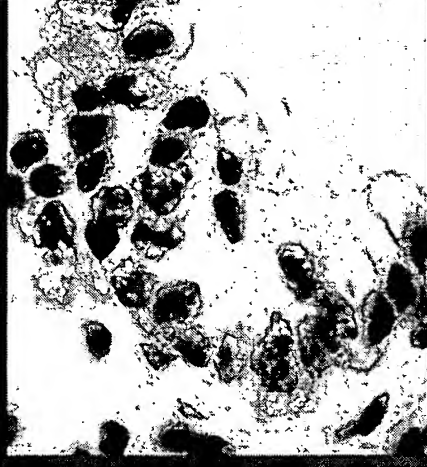
*Cftr*<sup>KO</sup>



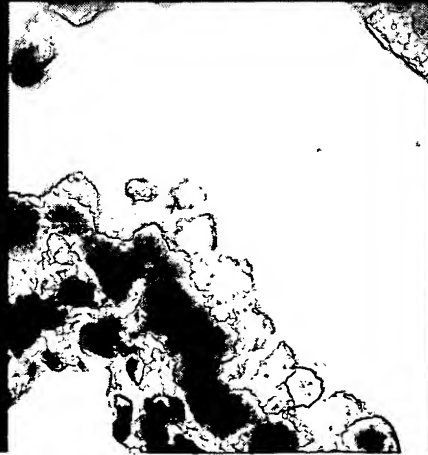
wt (B6)



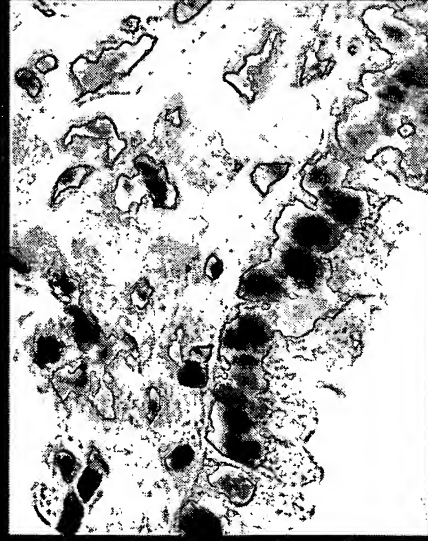
*Cftr*<sup>MHH</sup>



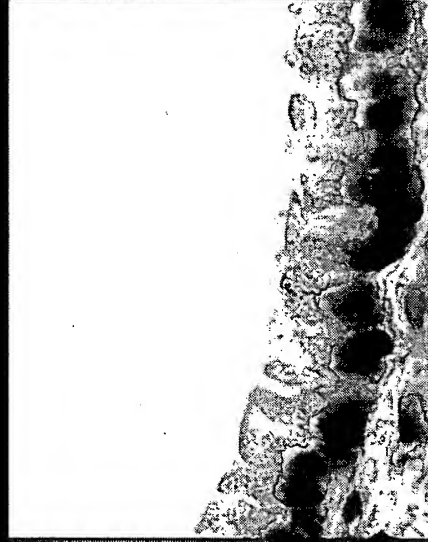
*Cftr*<sup>KO</sup> / *Smpd1*<sup>+/-</sup>



*Cftr*<sup>KO</sup> + Ami



*Cftr*<sup>MHH</sup> + Ami



*Cftr*<sup>KO</sup> + zVAD



Age [weeks]	wt	<i>Cfr</i> <sup>KO</sup>	<i>Cfr</i> <sup>KO</sup>	<i>Cfr</i> <sup>KO</sup> <i>Smpd1</i> <sup>+/-</sup>	wt (B6)	<i>Cfr</i> <sup>MHH</sup>	<i>Cfr</i> <sup>MHH</sup>	<i>Cfr</i> <sup>KO</sup>	<i>Cfr</i> <sup>KO</sup> zVAD
16	~0.5	~0.5	~0.5	~1.5	~0.5	~0.5	~0.5	~0.5	~0.5
24	~0.5	~1.5	~1.5	~1.5	~0.5	~0.5	~0.5	~0.5	~0.5
32	~0.5	~1.5	~1.5	~1.5	~0.5	~0.5	~0.5	~0.5	~0.5

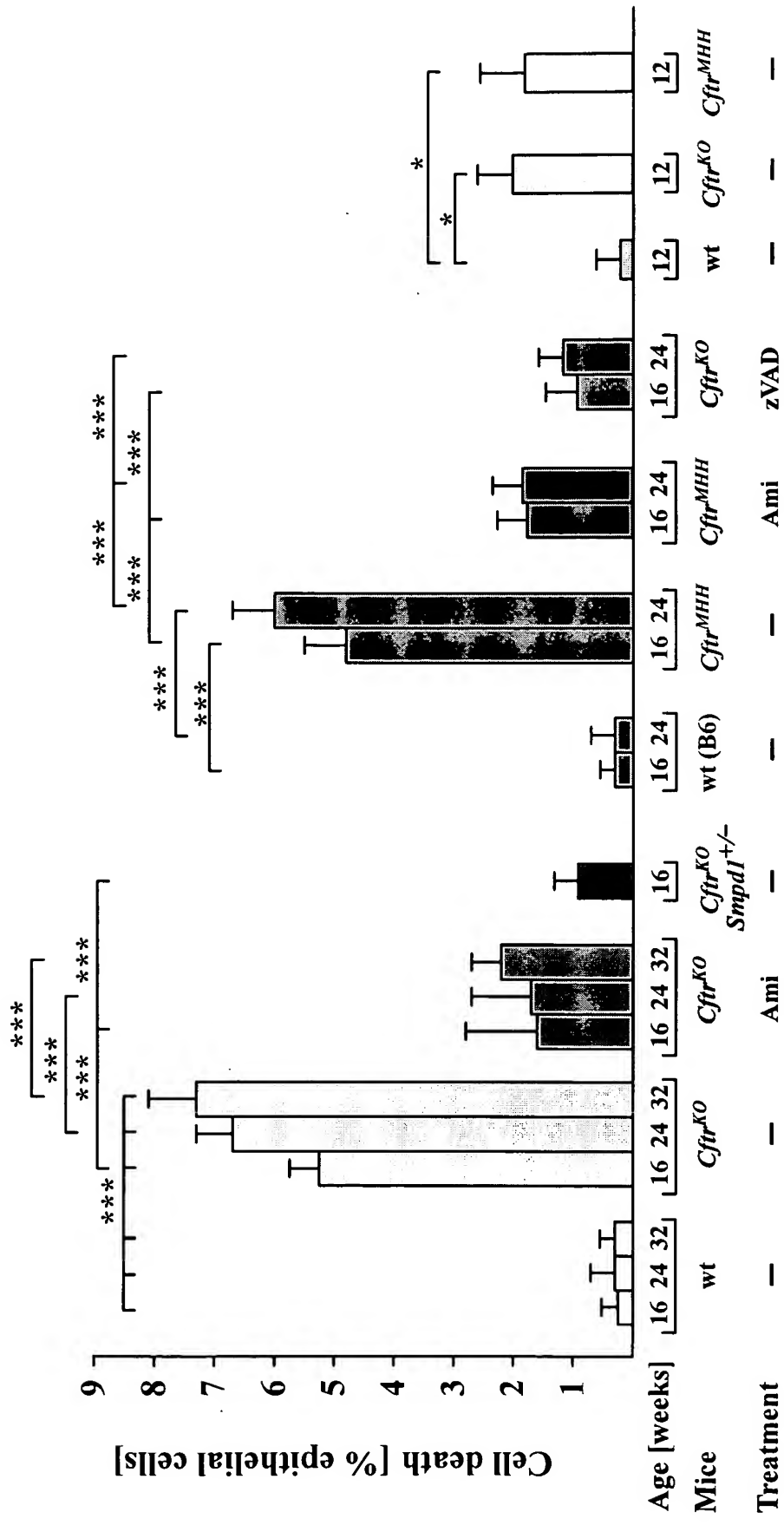
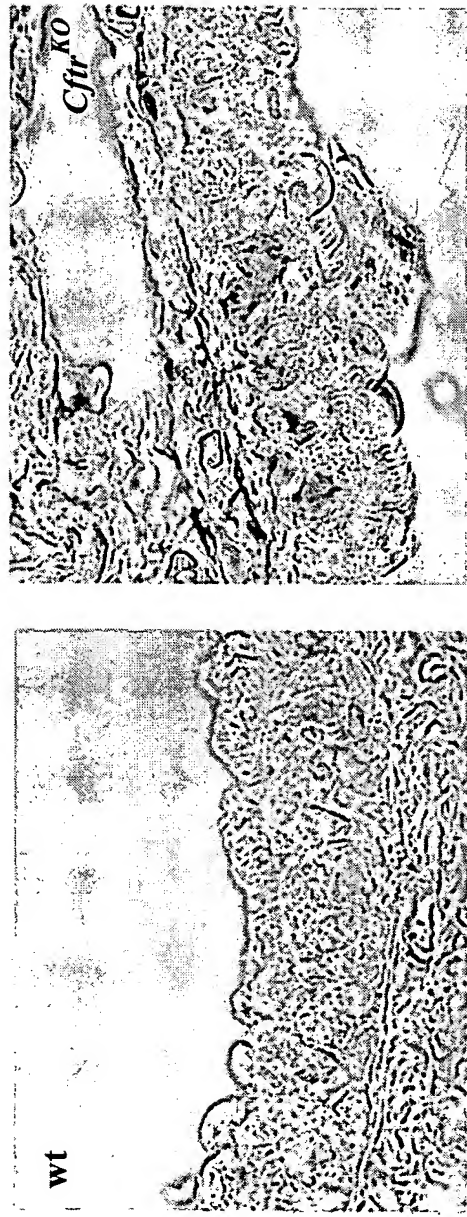
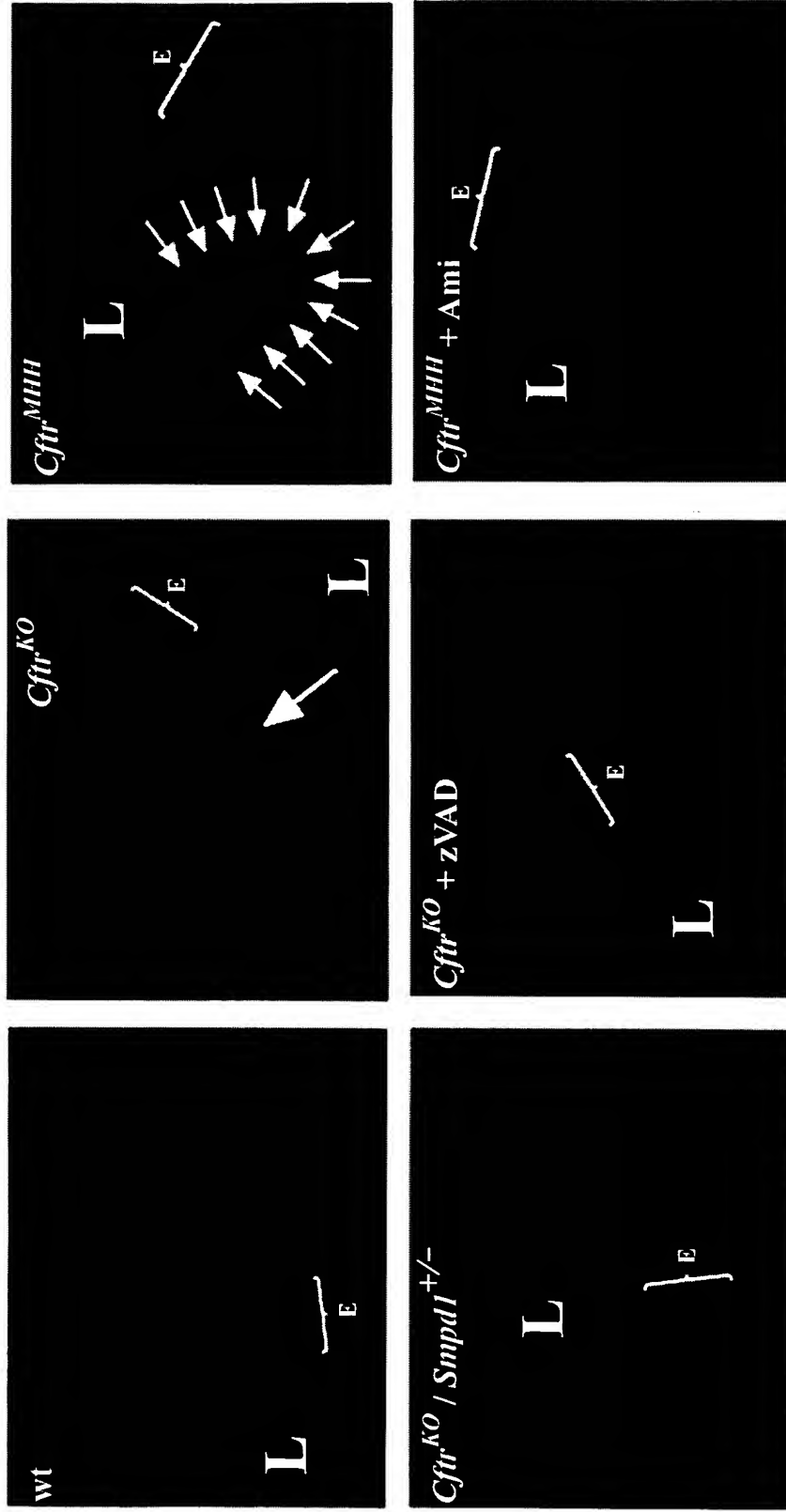


Fig. 5c



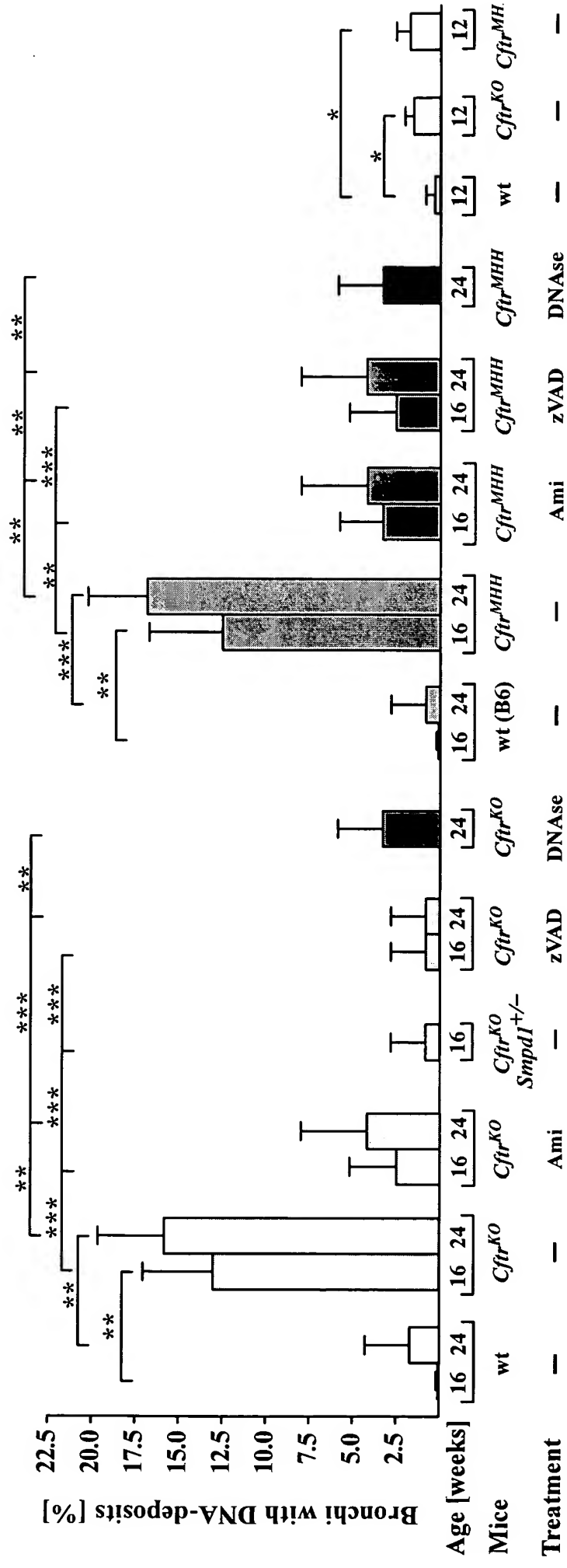
TUNEL

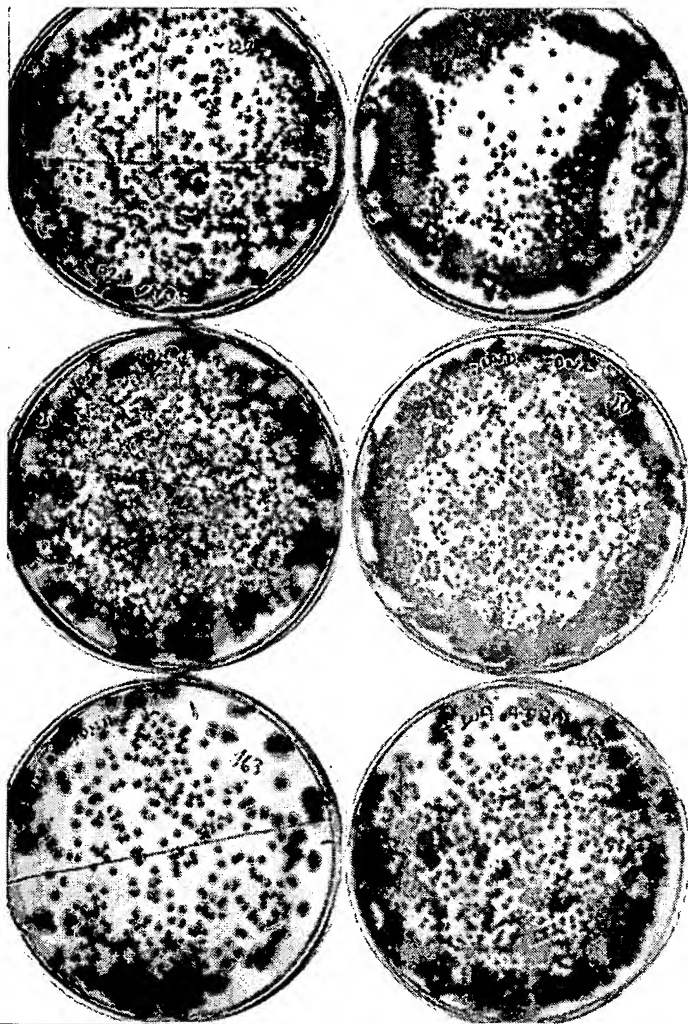


EtBr-  
staining

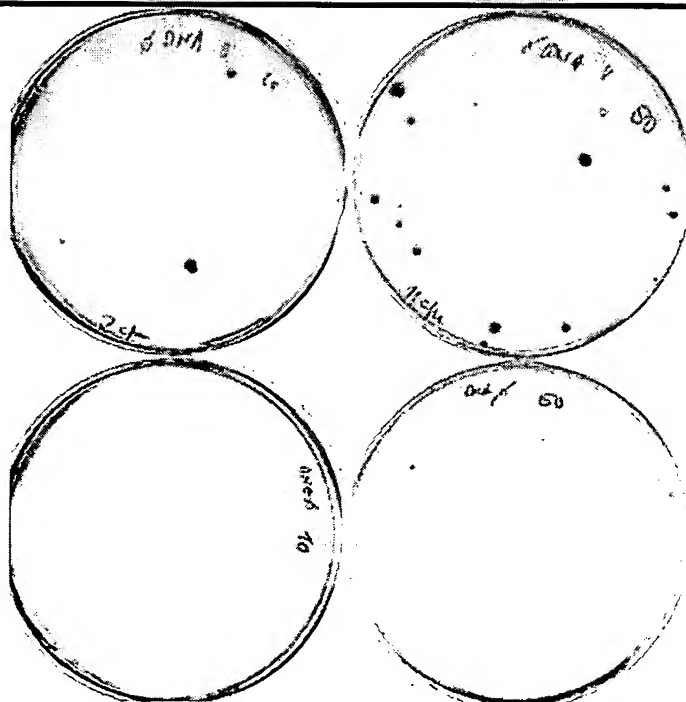
EtBr-  
staining

**Fig. 5d**





plus  
DNA



no  
DNA

**Fig. 6b**

**A549, no DNA**



**A549 + DNA**

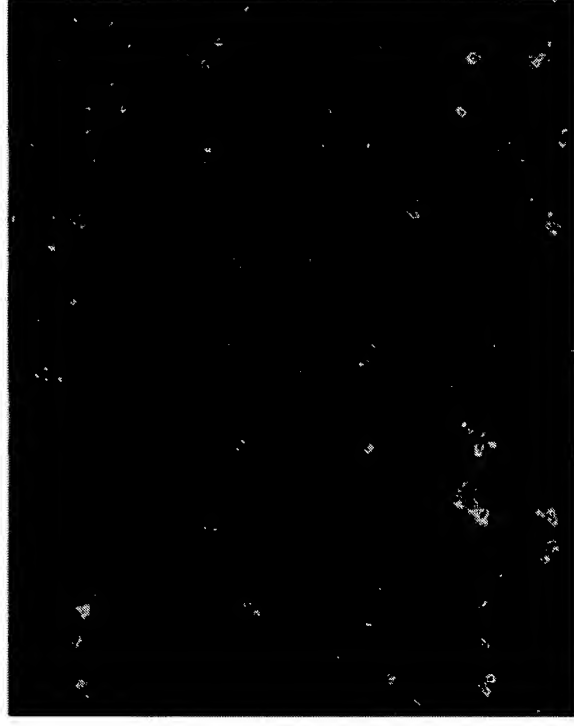


Fig. 6c

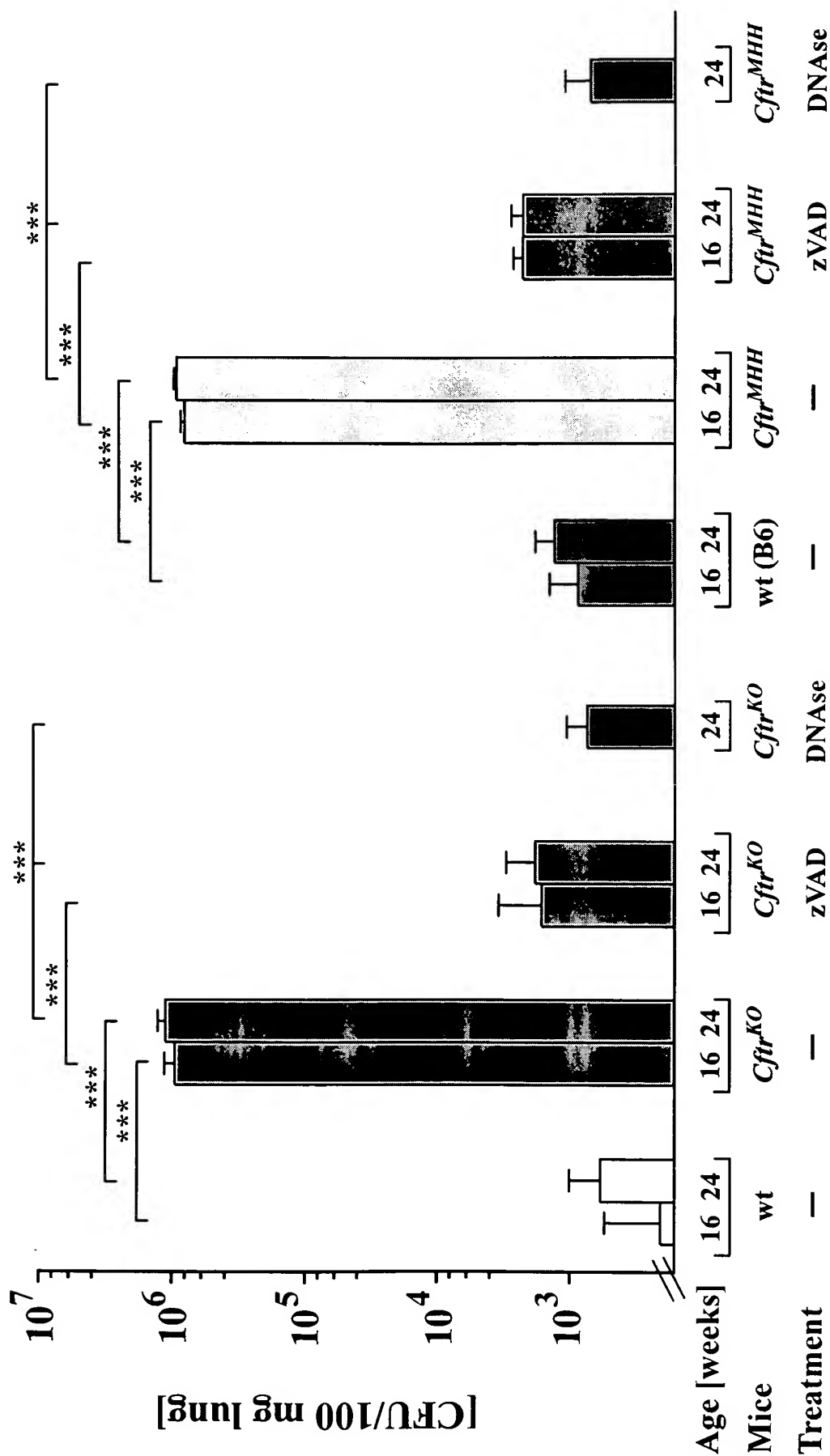


Fig. 7a

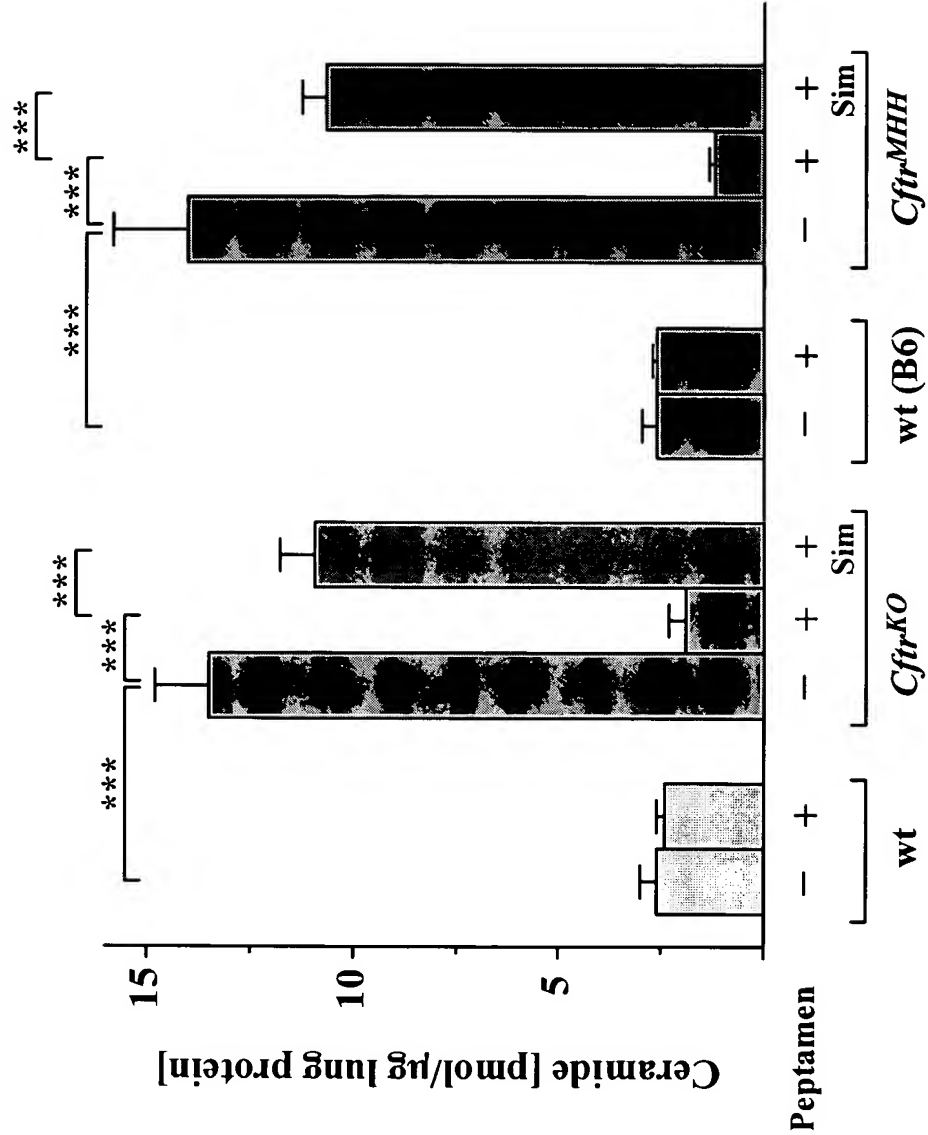




Fig. 10

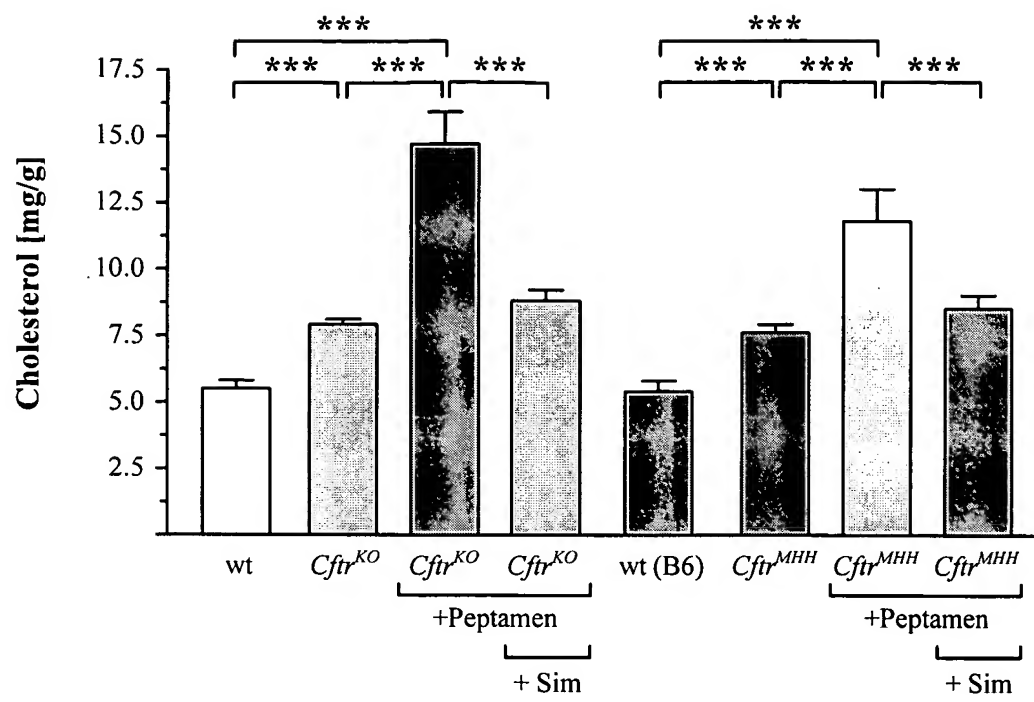


Fig. 7c

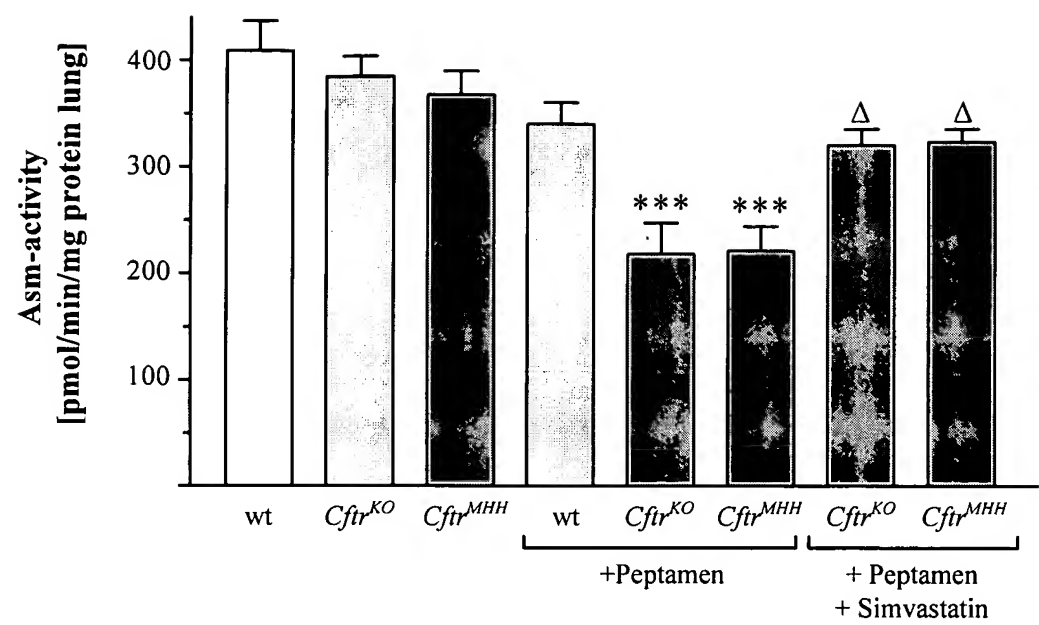


Fig. 7a

